BO1 OLDER DONORS TO RECIPIENTS OVER 60 YEARS OLD IN KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Background: The use of kidneys from old donors is controversial, although it has become generally accepted in several centers. Four years ago, a programme to transplant old donors to old recipients was set up in our center. The aim of the present work was to evaluate the outcome of this programme and to compare our results from those performed in other centers.
Methods: This is a retrospective study. From April 2011 to August 2014, 140 patients were transplanted with grafts from deceased donors aged 60 years and older (60–79). The end point was patient and graft survival. Graft and patients survival were calculated using Kaplan-Meier method. The mean lenghts of follow up were 21.8 ± 10.9 month.
Results: One hundred and thirty kidney transplants were performed. Median recipient and donor age were 67.1 ± 4.7 and 65.7 ± 5.5 years. After a median follow-up of 21.8 months, 17 of 140 patients died (12.1%). Twelve of seventeen patients died before of the first year of the transplant. The cause of death was because of cardiovascular complications (47%) and infectious diseases (53%). Twelve of the death patients died with functioning grafts. Patient survival rates are shown in Figure 1A. Death-censored and overall graft survival is shown in Figure 1B.
Conclusion: Fairly good short-term outcome of kidney transplant from donors aged 60 years and older can be achieved in elderly recipients with low comorbities.

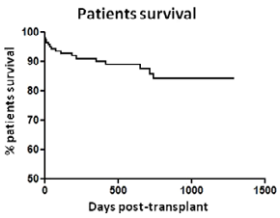

Figure 1A

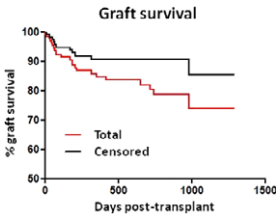

Figure 1B

BO2 OUTCOME OF EXPANDED CRITERIA (ECD) VERSUS STANDARD CRITERIA DONOR (SCD) KIDNEY TRANSPLANTS AFTER PRACTICE CHANGE: SINGLE CENTER EXPERIENCE

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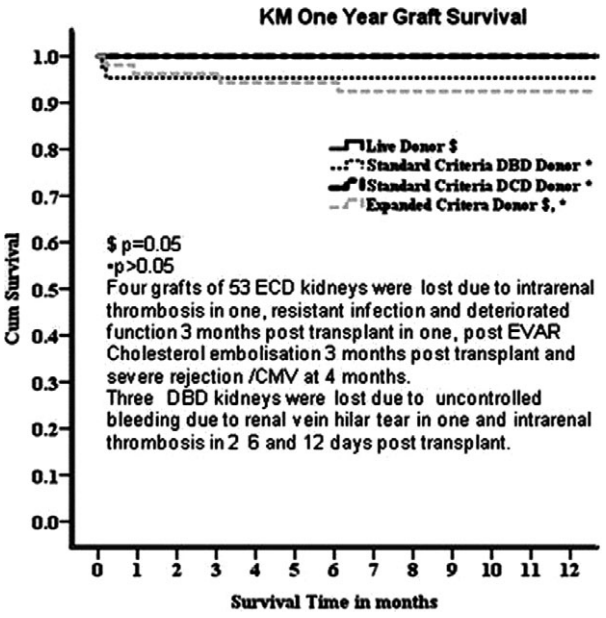
Background: While ECD kidneys are considered a source of kidney grafts, they are considered suboptimal compared to SCD. We present the outcome of ECD compared with SCD and live donor kidney transplants.
Subjects and Methods: All kidney transplants performed between Jan 2013–Feb 2014 were reviewed. This period reflects expanding the deceased donor acceptance criteria. A total of 165 kidney transplants included 49 live donors (LD), 63 SCD (43 DBD and 20 DCD) and 53 ECD (32 DBD and 21 DCD). Six ECD kidney pairs were utilised as Dual. ECD is defined as a donor ≥60 or 50–59 years old with at least two co-morbidities including hypertension, cerebrovascular accident (CVA) as a cause of death, and pre-retrieval creatinine >132.6 μmol/l
Results: There was no significant difference in gendre, age and co-morbidities between the 4 groups. There was no significant difference in cold ischemia time between SCD (DBD, DCD) and ECD groups. There was significant difference in delayed graft function (DGF) between ECD (17%) and LD (6%), ECD and DBD (11.6%) and ECD and DCD (40%) group ($p < 0.05$). There was no significant difference in 1, 3 and 6 months creatinine between ECD and DCD and DBD groups. There was a significant difference in 1 year graft survival at between ECD (92.5%) and live donor kidney transplants (100%) ($p = 0.05$) while there was no difference between ECD and DCD (100%) and DBD (95.3%) groups (Fig 1).
Conclusion: ECD kidney transplants offer a comparable outcome to SCD kidney transplants. DGF was noted to be higher in ECD and DCD groups but the majority of these kidneys recover.



BO3 NOMOGRAM OF RISK FACTORS FOR PREDICTING DELAYED GRAFT FUNCTION IN DONATION AFTER CARDIAC DEATH KIDNEY TRANSPLANTATION

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Background: Donation after cardiac death (DCD) kidney transplantation developed rapidly in China in recent years. However, delayed graft function (DGF) remains a critical problem for DCD kidney transplantation. It is important to identify the risk factors for predicting DGF before transplant.
Methods: We retrospectively collected clinical data of donors and recipients in 241 DCD kidney transplantation performed in our hospital from July 2011 to May 2014. All patients were followed up for at least 6 months. DGF after transplantation were recorded. Multivariate Logistic regression was used to investigate the independent risk factors for DGF. A nomogram for estimating the relative contribution of each risk factor was created.
Results: DGF occurred in 48(19.9%) patients. Multivariate Logistic regression showed that independent risk factors for predicting DGF included donor age, donor history of hypertension, donor death of cerebrovascular accidents, donor history of cardiopulmonary resuscitation, cold ischemia time, terminal serum creatinine, and previous transplant ($p < 0.05$). A nomogram quantifying the relative contribution of each risk factor was developed as tool for indentifying patients at risk for DGF. The predictive accuracy of DGF model was validated by use of data from Chinese Scientific Registry of Kidney Transplantation(CSRKT). The ROC curve showed the c index was 0.72.
Conclusion: The nomogram of risk factors for predicting DGF provides a useful tool for estimate the likelihood of DGF before DCD kidney transplantation. With this information, better allocation and treatment decision can be made before transplant.

BO4 HOW FAR CAN THE EXPANDED CRITERIA DONOR KIDNEYS TRANSPLANTATION BE SAFELY EXTENDED?

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Background: Expanded criteria donor(ECD) kidneys are currently defined as donor kidneys from all deceased donors over 60 years old or aged 50–59 years with a minimum of two additional co-morbidities of either cerebrovascular cause of death, serum creatinine over 1.5 mg/dl and/or hypertension. It is agreed that ECDs have worse graft survival than standard criteria donor (SCD) kidneys. We aim to quantify the potential difference between the SCD kidney from donors older than 40 years of age and the ECD kidneys, which were transplanted in our centre.
Methods: Analysing a prospectively collected data, we reviewed all deceased kidneys transplanted between October 2010 and June 2014. Graft failure was assessed at 3, 6, and 12 monthly intervals then annually. We defined a graft failure by an eGFR <15 and or the need for restarting or initiating renal replacement therapy. Statistically comparing two groups at a time for rate of delayed graft function (DGF), primary non-function (PNF), and graft failure at 1 year, three groups were compared, i.e SCD, ECD up to 70 years of age (ECD70). We used Chi-Square test (2-sided) for statistical analysis.
Results: 378 transplant procedures were performed including 37 dual kidney transplants. 69.9% of the recipients and 52.8% of the donors were males. Mean recipients' age was 58.5 years (21.9–80) and mean donors' age was 60.9 years (40–80.5). There was 113 SCDs, 129 ECDs70. There was no statistical difference between any of the groups on dual comparison ($p = 1$, 0.260, and 0.268 for SCD versus ECD70 and EC70 respectively). Although ECD>70 showed a higher rate of DGF (77.6% vs. 65.1% and 50.4% for ECD70 was comparable to both other groups in 1 year graft failure rate (1.5, 5.4 and 5.3% for ECD>70, ECD<70 and SCD respectively) and return or initiation of renal replacement therapy (3, 7.8 and 5.3% respectively).
Conclusion: One-year graft survival in older age group of ECDs could be comparable to younger ECD group and SCDs.

BO5 EVEROLIMUS VERSUS MYCOPHENOLATE FOR RECIPIENTS OF KIDNEY TRANSPLANTS FROM EXPANDED CRITERIA DONORS (ECD) RECEIVING ANTI-THYMOCYTE GLOBULIN AND TACROLIMUS

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Introduction: Recipients of kidneys recovered from expanded criteria donors are at higher risk to develop delayed graft function and acute rejection, leading to inferior graft function and graft survival. The ideal immunosuppressive regimen for these recipients has not been defined. Our study compared the efficacy and safety of everolimus or mycophenolate sodium in ECD kidney transplant recipients receiving induction therapy with anti-thymocyte globulin, tacrolimus and prednisone.
Methods: This is a prospective, randomized, single center study designed to enroll 200 patients (1:1) to receive Induction therapy with anti-thymocyte globulin, prednisone, delayed introduction of tacrolimus (day 7) and everolimus (EVR group) or mycophenolate sodium (MPS group). This preliminary analysis was performed with 84 randomized patients ($n = 44$, EVR and $n = 40$, MPS) with a median follow up of 7 months. Preemptive strategy was use for CMV infection.
Results: There were no differences in mean kidney donor profile index (KDPI, 89 ± 7 vs. 88 ± 11%) and mean kidney donor risk index (KDRI, 1.6 ± 0.2 vs. 1.7 ± 0.1) comparing EVR and MPS groups, respectively. There were no differences in main demographic characteristics except the incidence of diabetes mellitus (EVR, 36% vs. MPS, 10%). There was no difference in incidence of delayed graft function (64 vs. 70%, $p = 0.537$) but a tendency to lower duration in DGF (9.8 ± 7.5 vs. 6.5 ± 5.1 days, $p = 0.057$) in MPS group. The incidence of first CMV infection was lower in EVR group (13 vs. 87%, p = 0,000). Furthermore, 43% patients in MPS ($n = 15$) developed at least one recurrent event of CMV infection. Higher incidence of treated acute rejection (36 vs. 23%, $p = 0.165$) or treated biopsy confirmed acute rejection (16 vs. 8%, $p = 0.235$) was observed in the EVR group. No differences in mean estimated glomerular filtration rate (MRDR, 41 ± 19 vs. 46 ± 14 ml/min, $p = 0.285$) were observed at 6 months. Treatment discontinuation occurred in six patients in EVR and 12 in MPS group.

BO6 EX VIVO PERFUSION CHARACTERISTICS OF DCD KIDNEYS PREDICT LONG-TERM GRAFT SURVIVAL

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Background: Ex vivo cold perfusion is used in our unit for kidneys donated after cardiac death (DCD). The machine has 2 modes, continuous and pulsatile. Perfusion flow index (PFI) which equals to flow divided by systolic pressure of machine, resistance (RT) and perfusate Glutathione S Transferase (GST) are measured to assess graft viability and can predict early function.
Aim: To determine whether machine perfusion parameters predict long-term graft survival.
Method: All DCD kidney transplants performed between 2003 and 2015 in our unit are included in this study. The exclusion criteria were unavailable data from records, kidneys not machine perfused on machine, dual transplantations. 241 kidney transplants were included in the final analysis (155 pulsatile and 86 continuous perfusion). Demographic data, warm ischemia time, cold ischemia time, total ischemia time, donor hypertension (HT), graft function and survival and machine perfusion parameters after 3 h were analysed. Machine parameters are grouped by tertiles (high middle and low). Estimated glomerular filtration rate (eGFR) was calculated at discharge, 12th months, then yearly after transplantation.
Results: PFI and RT were significantly associated with donor age but not donor hypertension. RT was higher in kidneys from female donors. There was a significant association with PFI and graft survival ($p = 0.026$) with 20% superior graft survival at 5 years between kidneys with low compared with high PFI (Figure 1). There was no relationship between RT or GST and graft survival. eGFR at 12th months after transplantation was statistically higher in patients with good PFI values compared to other PFI groups.
Conclusion: PFI, measured during ex vivo cold machine perfusion, is predictive of long term survival. PFI is also associated with donor age. Further analysis is required to determine if the relationship between PFI and graft survival is explained by the association of both variables with age.

BO7 CLINICAL OUTCOMES IN RECIPIENTS OF LIVING DONOR KIDNEY TRANSPLANTS FROM ELDERLY DONORS

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Background: Living donor kidney transplantation (LDKT) from elderly donors is controversial as graft function remains unclear. We evaluated the clinical outcomes of LDKT recipients from elderly (≥60 years) donors.
Methods: Between January 2010 and December 2013, 46 patients underwent LDKT at our center. Patients were grouped into an elderly donor (ED; LDKT from donors ≥60 years old; $n = 20$) and a normal donor group (ND; LDKT from donors <60 years old; $n = 26$). Baseline data, graft function, and immunosuppressant use were compared.
Results: Patients in the ED and ND groups were 44.1 ± 11.4 years and 65.2 ± 4.0 years old, respectively. The patient and graft survival rates were 100%. No significant difference in the donors' preoperative estimated glomerular filtration rates was observed between the two groups (ED vs. ND: 82.5 ± 13.6 vs. 92.4 ± 19.6 ml/min, respectively; $p = 0.073$). Preoperative creatinine clearance (ED vs. ND: 93.2 ± 19.1 vs. 108.7 ± 20.5 ml/min, respectively; $p = 0.01$) and the proportion of patients who were steroid-free within 1 year after the LDKT (ED vs. ND: 4/20 [20.0%] vs. 16/26 [61.5%], respectively; $p < 0.01$) were however significantly different between the 2 groups. A total of 35.0% (7/20) and 7.7% (2/26) of ED and ND patients, respectively, required medications for cytomegalovirus infections 1 year after the LDKT ($p = 0.023$). Although serum creatinine levels within 1 year after the LDKT were significantly higher in the ED than in the ND group, levels during the 2nd and 3rd year after the LDKT were no longer significantly different (ED vs. ND at 2 years: 1.29 ± 0.44 vs. 1.62 ± 0.38, respectively; $p = 0.054$; 3 years: 1.42 ± 0.44 vs. 1.46 ± 0.38, respectively; $p = 0.66$).
Conclusion: In this study, LDKT from elderly donors was relatively safe, but initial lower renal function and cytomegalovirus infection were seen. Careful selection of elderly donors and infection prophylaxis after LDKT may result in successful outcomes.

BO8 EVEROLIMUS AND LOW DOSE CYCLOSPORIN PROVIDE BETTER GRAFT SURVIVAL IN THE LONG TERM FOLLOW-UP OF RENAL TRANSPLANT RECIPIENTS FROM EXPANDED CRITERIA DONORS (ECD)

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Azienda Ospedaliera Universitaria Senese

Background: Different immunosuppressive regimens have been explored to avoid nephrotoxicity with CNI dose minimization. The impact of Everolimus therapy in combination with low-dose Cyclosporin on clinical outcome beyond 10 years after renal transplant is still not well defined.
Methods: Between 2000 and 2014 146 kidney transplant patients were de novo immunosuppressed with Everolimus and reduced dose Cyclosporin, mantained for the entire length of follow-up (group 1). A control group of 123 patients received standard dose Cyclosporine + Mycophenolate Mofetil (group 2). All the patients were treated with standard steroid therapy and Basiliximab induction. We examined retrospectively the graft and patient survival rate in the total population and in the sub-group receiving kidneys from Expanded Criteria

Donors (ECD). We evaluated mean creatinine levels, creatinine clearance and complication rates.
Results: The patient survival rate was comparable in the two groups, 96.4% vs. 95% at year 1, 91.9% vs. 95% year 3, 89.9% vs. 92.8% year 5 and 78.8% vs. 87% year 10 ($p = 0.159$). The graft survival rate (death censored) didn't show differences at long-term follow-up, but was higher in the sub-group of ECD kidneys recipients treated with low-dose Ciclosporin + Everolimus (Table 1).

	Year 1	Year 3	Year 5	Year 10	p-Value
All patients (no. 269)					
Group 1: CsA + Everolimus (no. 146)	90.8%	87.1%	77.8%	65.9%	p = 0.745
Group 2: CsA + MMF (no. 123)	90.8%	85.3%	80.7%	68.9%	
ECD donors only (no. 151)					
Group 1: CsA + Everolimus (no. 102)	89.8%	83.0%	75.0%	**71.1%**	p = 0.130
Group 2: CsA + MMF (no. 49)	84.8%	75.8%	70.1%	**55.6%**	

The renal function (mean creatinine and clearance levels) was similar in the two groups, as well as the acute rejection episodes (51 vs. 44). The most frequent serious adverse events were bacterial and viral infections, 42 vs. 58 cases, neoplasms 13 vs. 3, skin cancers 3 vs. 6, major cardiovascular events 7 vs. 8. Hyperlipidemia was only present in 4 cases in the group 1.
Conclusion: The use of Everolimus and low-dose Cyclosporin is a safe treatment of de novo renal transplant recipients, that shows a better graft survival at long term follow-up for the high risk group of ECD kidneys recipients. The immediate introduction of Everolimus does not increase the post-operative risk of wound healing or other complications.

BO9

CLINICAL OUTCOME AFTER RENAL TRANSPLANTATION WITH DONORS OVER 60 YEARS OF AGE

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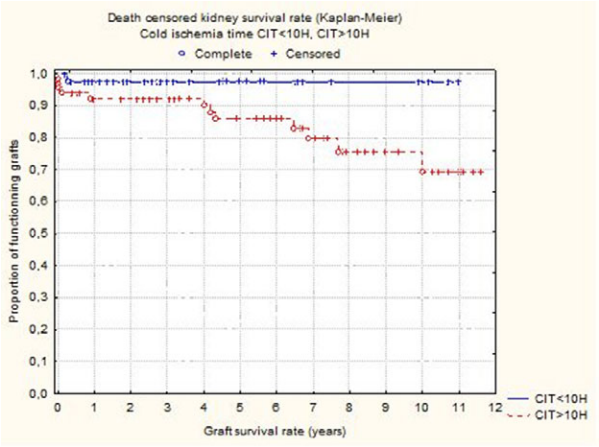
Universite de Montreal

Introduction: Transplantation of kidneys from donors over 60 years of age (D > 60) remains controversial regarding the early and late outcome.
Methods: We reviewed 559 consecutive deceased kidney transplantations performed between January 2003 and September 2014, excluding combined transplantations.
Results:

	Group D < 60	Group D > 60	
Number	452	107	
Recipient age (years)	49 ± 12	54 ± 12	<0.000005
Donor age (years)	41 ± 14	65 ± 3	
Donor creatinine clearance	123 ± 48	106 ± 34	<0.002
Donor Obesity	19%	14%	
Donor HTA	8%	22%	
Donor tobacco use	23%	20%	
Cerebrovascular accident as cause of death	55%	77%	
Cold ischemic time (min)	748 ± 288	644 ± 320	
PRA (%)	17 ± 26	16 ± 25	
No. of HLA mismatches	3.2 ± 1.7	3.4 ± 1.7	
Delayed Graft Function	30%	48%	

In the group of patients receiving a kidney graft from a donor younger than 60 years, the patient survival rate at 1, 5 and 10 years was respectively: 98%, 91% and 83% and the graft survival rate was 93%, 83% and 71%. In the other group (D > 60), the patient survival rate was respectively: 99%, 90% and 76% and the graft survival rate was 98%, 89% and 76% (NS between the 2 groups). The death censored graft survival rate of kidneys with a shorter cold ischemic time than 10 h was 98% at 10 years.
Conclusion: In our experience, an older donor is a valuable source of kidney. Even if a delayed graft function usually occurs, a long term survival can be achieved. A good selection of donors: a renal biopsy is mandatory before accepting those kidneys for transplantation, and a short cold ischemic time play probably an important role.



BO10

ARE KIDNEYS DONATED AFTER BRAIN DEATH (DBD) BETTER THAN KIDNEYS DONATED AFTER CIRCULATORY DEATH (DCD)?

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Renal Transplant Unit, Glasgow

Introduction Kidneys donated after circulatory death (DCD) have been considered more vulnerable to added physiological insult and thus at greater risk of poorer outcomes than kidneys donated after brainstem dead donors (DBD). However, the reversal of this has been subjectively observed. The aim of this study was to determine if the outcome by donor type is poorer following circulatory death than after brainstem death, particularly in the group with added insult leading to delayed graft function (DGF).
Methods: Retrospective analysis of all adult renal transplantation, over a 4 year period (2011–2014), was performed. Baseline demographic characteristics and outcomes were compared for DBD and DCD transplants. Outcome measures included serum creatinine at 1 year and biopsy proven acute rejection (BPAR) rates. The rates of DGF and their outcomes were also analysed.
Results: Two-hundred-and-fifty deceased donor transplants were identified; 90 DCD and 160 DBD. Extended criteria donor organs were utilised in 36% of cases. The DBD and DCD case mix was not significantly different in respect to donor or recipient. The outcomes were not statistically different between DCD and DBD donated kidneys (serum creatinine at 1 year (128.6 ± 4.83 vs. 144.6 ± 6.77), BPAR (13.1% vs. 8.9%, $p > 0.05$) and incidence of DGF (47.47% vs. 48.10%). The DGF outcomes differed by type of donor: a statistically significant lower creatinine at 12 months was observed for a DCD kidney with DGF than for an equivalent DBD (134.83 ± 6.12 vs. 167.85 ± 11.39). This pattern was the same for all categories of kidney: standard (108.08 ± 5.58 vs. 148.21 ± 11.80) and extended (166.62 ± 7.99 vs. 201.18 ± 22.3) criteria DCD's with DGF, and for DCD >65 years with DGF (171.15 ± 22.42 vs. 193.75 ± 20.63).
Conclusion: A contemporary DCD is equivalent to a present-day DBD kidney. However, in the context of DGF, despite needing prolong HD, DCD outcomes are better.

025 LIVER

BO11 EARLY ALLOGRAFT DYSFUNCTION LEADING TO GRAFT FAILURE WITHIN 3 MONTHS POST LIVER-TRANSPLANTATION

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Introduction: Early allograft dysfunction (EAD) adds burden to transplant programmes, whilst the aetiology of EAD is predictable in some cases, in a proportion of these cases definitive cause cannot be identified leading to eventual graft/patient loss. Severe EAD is usually associated with overlapped histological findings of rejection and biliary features, which are often difficult for interpretation. We review the outcome of this group and the strategies of management.
Material and Methods: Of 1583 liver transplants performed at our institution in the last 10 years, graft failure occurred within 3 months in 131 (8.2%) cases; excluding cases of primary non function/hepatic artery thrombosis, definitive diagnosis of sepsis and those due to vascular problems ($n = 84$), a total 45 patients [54(17–71) years] had severe EAD and graft failure. Demographic characteristics, allograft biopsies, radiological investigations and clinical outcome were analysed.
Results: All patients had un-resolving liver biochemistry [AST 205(6–10160) IU/l, bilirubin 260 (4–975)μmol/l, INR 1.1 (0.8–6.9). Doppler scan was normal in all cases and 35 (78%) recipients had at least one allograft biopsy [2 (1–10)]. Histologically, rejection and biliary injury features were observed in 26 (74%) and 25(71%) cases respectively and, overlapped in 19 (54%). However only in eight patients biliary anatomy was studied in detail and all reported biliary stricture. The majority ($n = 39$; 87%) died within 32 (10–91) days, only survivors ($n = 6$; 13.3%) were from re-transplantation ($n = 2$) or biliary intervention ($n = 4$).
Discussion: EAD significantly influence patients/allograft outcome. Histolgically, rejection seems to overlap with biliary strictures in number of cases; hence allograft biopsy with signs of rejection shouldn't be a reason to overlook biliary problems, in particular when biliary features are present. Only extensive radiological investigation and intervention or re-transplantation salvages grafts or saves patients.

BO12 THE EDINBURGH LIVER FUNCTION (ELF) SCORE RAPIDLY AND OBJECTIVELY IDENTIFIES SEVERE GRAFT DYSFUNCTION AFTER LIVER TRANSPLANTATION

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Introduction: Graft dysfunction after liver transplantation is common. Severe dysfunction requires early recognition and multiple organ support to ensure survival. By contrast, Primary Graft Non-Function (PNF) is rare, but invariably fatal without urgent re-transplantation. In clinical practice, the early diagnosis of PNF as opposed to severe dysfunction can be extremely difficult. Currently, there are no reliable scoring systems to distinguish graft dysfunction and non-function based on routine clinical data.
Aim: To derive a statistical model describing the normal distribution of liver function in the first 48 h after liver transplantation.
Materials and Methods: Routine clinical data were recorded prospectively and analysed retrospectively in 169 control patients and eight patients with PNF in the Scottish Liver Transplant Unit. Regression techniques were used to construct a predictive model describing post-operative liver function, derived from indices identified from correlational analyses. Clinical teams did not have access to the ELF score.
Results: Post-operative trends in bilirubin, lactate and prothrombin time comprised the model. Z scores for these analytes at different time points were combined to give the Edinburgh Liver Function (ELF) Score. 9/177 patients developed an ELF score >1.96 at 12–48 h post-transplant. Of these, 1 died, and 6 were listed for super-urgent re-transplantation. One improved and was de-listed with a falling ELF score. One was considered for re-listing, however, the patient improved. One had been anticoagulated, giving a false positive. No PNF cases were missed by the ELF score. An ELF score >1.96 had a positive predictive value for death or re-listing of 87.5% and a negative predictive value of 100%.
Conclusions: The ELF score is a simple and rapid technique. ELF score may focus attention on patients with severe liver dysfunction objectively, allowing targeted intervention and the earliest possible re-transplantation.

BO13 REDUCING THE RISK OF EARLY ALLOGRAFT DYSFUNCTION IN LIVER TRANSPLANT RECIPIENTS BY ACTIVATION OF THE PREGNANE X RECEPTOR (PXR)

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Introduction: There has been increasing interest in the pregnane X receptor (PXR) in recent years as a promising drug target for the treatment of inflammatory liver disease. Our group has previously demonstrated that activation of the PXR reduces oxidative stress and fibrosis in a rat model of liver ischaemia-reperfusion injury. The aim of this study was to investigate the effect of PXR activation on early graft function in clinical liver transplantation.
Methods: Data was collected retrospectively for all patients receiving deceased donor liver transplants in a major transplant centre in the UK over the past 3 years. Patients were divided into high and low PXR activation groups based on the potency and number of PXR-activating drugs administered over the first week of transplantation. Early allograft dysfunction (EAD) was measured using a validated scoring system and was compared between the two groups in addition to graft and patient survival.
Results: Eighty three patients were considered eligible for inclusion in this study ($n = 43$ and 40 in the low and high PXR activation groups respectively). The incidence of EAD was significantly higher in the low PXR activation group (30.2% vs. 10% in the high PXR activation group; $p < 0.05$). No significant differences in graft or patient survival were demonstrated in this small cohort.
Conclusion: Activation of the PXR resulted in a reduction in EAD following liver transplantation in the clinical setting; consistent with our previous results in the animal model. Our findings have important implications for the potential reduction of graft loss following DCD liver transplantation.

BO14 DOES HEMODYNAMIC STABILITY CORRELATE WITH LIVER FUNCTION RECOVERY IN EARLY POST-TRANSPLANTATION PERIOD?

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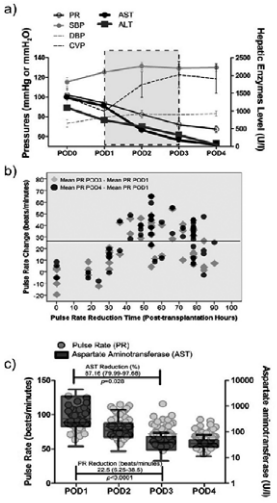
Background: Hyperdynamic circulation due to portal hypertension and cirrhosis begin to normalize soon after the liver transplantation. We studied the probable relationship between hemodynamic changes and liver function tests during the early post transplant days.
Methods/Materials: In the present retrospective cross-sectional study, 57 patients who underwent liver transplantation between January 2012 and January 2013 at Imam Khomeini hospital complex were investigated. During the first 11 days following the surgery, serum levels of aspartate transaminase (AST), alanine transaminase (ALT), and bilirubin as well as prothrombin time (PT) were measured daily, and hemodynamic parameters at 6 h intervals.
Results: A significant decrease in the serum levels of AST ($p = 0.028$), ALT ($p < 0.00001$), and bilirubin ($p < 0.00001$) as well as PT ($p = 0.002$) was observed. Hemodynamic stability was achieved during the first 72 h following the surgery, and a significant decrease in the heart rate (HR) was observed in concordance with significant increase in mean arterial pressure and central venous pressure (CVP). The HR reduction of patients (lower than 87 beats per minute) was associated with the maximal increase in their CVP and mean arterial pressure during the first 24–72 post-transplant hour ($p < 0.00001$). These hemodynamic changes were also associated with a dramatic decrease in the serum levels of liver enzymes during 24 and 72 after the surgery. In all patients who experienced a post-transplant HR of <87 beats per minute, AST levels dropped below 180 IU/l in the next 24 h.



a) Hemodynamic characteristics of patients undergone liver transplantation determines the hepatic enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, especially in postoperative days (POD) 1 to 3 (gray box). b) The mean pulse rate (PR) changes of patients are displayed along with the time of dramatic PR reduction. Mean PR reductions from POD1 to POD3 and POD1 to POD4 was median (interquartile range) 28.75 (8.5-39.75) beats/minutes and 30.25 (11.75-42.17) beats/minutes. c) Pulse rate (PR) reductions median (interquartile range) 22.5 (6.25-38.5) beats/minutes were concomitant with AST reduction of 87.16% (79.99%-97.68%) from POD1 to POD3. Normally distributed data are shown by mean (95% confidence interval) and are tested by repeated measures ANOVA; non-parametric data are displayed by median (interquartile range) and are tested by Friedman test. $p<0.05$ is considered statistically significant.

Conclusion: We found a significant relationship between early post-transplantation hemodynamic stability and liver function recovery. Post-transplantation heart rate reduction as a sign of hemodynamic stability and indicator of improved liver function may guide surgeon for better management of fluid therapy and prevention of volume overload and pulmonary edema.

BO15 POST REPERFUSION TISSUE OXYGEN SATURATION IS ASSOCIATED WITH EARLY ALLOGRAFT DYSFUNCTION IN CLINICAL LIVER TRANSPLANTATION

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Background: After cold preservation of solid organs microcirculatory reperfusion is key for sufficient oxygen and nutrient supply, therefore for successful transplantation. This study aimed to analyze hepatic microcirculation after liver transplantation and evaluate the predictive potential on the outcome in an extended criteria donor cohort.
Patients and Methods: Single center prospectively collected pre- intra- and postoperativ data (OPAL study/ 01/11–12/13) of 116 extended criteria donor liver transplantations were utilized. One hour after allograft reperfusion oxygen saturation (SO2), relative capillary hemoglobin concentration (rHB) and blood flow were measured on the surface of the allografts by combination of laser-doppler-flowmetry and tissue-spectrometry (O2C, LEA Medizintechnik, Germany). All data were correlated with occurrence of Early Allograft Dysfunction by univariable/multivariable logistic regression.
Results: The median DRI was 1.8. 60.3% of recipients were male with a median age of 54 (23–68) years. Rate of EAD was 22.4% and 3 months survival was 90.5%. SO2, rHB and blood flow was median 78 (29.5–95.8)%, 55.6 (16.8–74.8) AU and 110.1 (35.8–406.8)AU, respectively. After adjustment for confounders by multivariable analysis tissue SO2 ($p = 0.01$), recipient BMI ($p = 0.003$), donor last ALT ($p = 0.02$) and portal flow after reperfusion ($p = 0.01$) were identified as independent risk factors for development of EAD.
Conclusion: Intraoperative non-invasive measurement of tissue oxygen saturation can display additional information for the prediction of development of EAD after transplantation. This parameter might therefore help in the assessment of allograft reperfusion quality and support further clinical decision making.

BO16 INCIDENCE OF POSTHEPATECTOMY LIVER FAILURE AS DEFINED BY ISGLS AMONG LIVING LIVER DONORS

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Background: Although studies have reported donor morbidities, postoperative deterioration of donor liver function, which could lead to posthepatectomy liver failure (PHLF), has not been assessed.
Methods: We analyzed the incidence of PHLF as defined by the International Study Group of Liver Surgery (ISGLS-PHLF) among 257 living donors. ISGLS-PHLF is defined by an increased international normalized ratio (INR) and hyperbilirubinemia on or after postoperative day 5.
Results: ISGLS-PHLF was identified in 21 (8%) donors. Eighteen (7%) donors were categorized as Grade A (requiring no clinical management) and three (1%) as Grade B (requiring non-invasive treatment). Without ISGLS-PHLF, the average hospital stay was 15 ± 1 days, and this duration was extended with increasing grades of ISGLS-PHLF ($p = 0.03$). Univariate analysis identified right hepatectomy as a significant factor for ISGLS-PHLF ($p = 0.02$), and multivariate analysis identified right hepatectomy and operation time ($p = 0.01$). Among 176 right lobe donors, univariate analysis identified operation time as a significant factor ($p = 0.002$), and multivariate analysis identified operation time ($p = 0.01$) and donor age $\leq$50 years ($p = 0.04$). Further analysis revealed that even with no selection bias for younger donors with larger graft volumes among right lobe donors ($p = 0.11$), younger donors showed increased INR compared with older donors preoperatively ($p = 0.0012$) and on postoperative day 10 ($p = 0.02$). This was also observed for left lobe younger donors preoperatively ($p = 0.01$) and on postoperative day 7 ($p = 0.01$).
Conclusions: To prevent potential PHLF and achieve zero mortality in living donors, selection of a right lobe graft should be carefully discussed even with younger donors.

BO17 ASSOCIATION OF RS913930 GENOTYPES OF TLR-4 GENE WITH EARLY GRAFT DYSFUNCTION AFTER LIVER TRANSPLANTATION

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Several risk factors of early allograft dysfunction (EAD) in LTx are well described. Nevertheless, a proportion of EAD occurs beyond of known factors. In a murine liver, TLR4 promotes injury after I/R (J.D.Ellett et al. Liver Transplant. 2011). A significant association of minor allele of some TLR4 SNPs was found with all cause liver graft failure after LTx (W.S. Oetting et al. Liver Transplant. 2012). To date no genotypic association in European pts is reported.

Aim: to assess the association of TLR-4 genotypes in clinically significant SNPs rs11536865, rs913930 and rs5030717 with EAD after LT.

A case-control study was conducted. Period of study: Feb 2013–Oct 2014. Inclusion criteria: LT from DBD donor. Exclusion criteria: LDLT, reduced graft, recipient age <18. Blood samples were obtained from 98 DBD donors before multiorgan procurement. SNP were determined and analysed in stored samples of 40 random donors. Genomic DNA was isolated from blood cells with Thermo Scientific Genomic DNA Purification Kit. SNPs of TLR-4 rs11536865 (G/C), rs5030717(A/G) and rs913930 (T/C) were determined by sequencing PCR (Big Dye Terminator v3.1 Cycle Sequencing Kit). EAD was defined according to K.M.Olthoff (Liver Transpl. 2010).
Results: 32.4% of rs913930 and 15% of rs5030717 samples were heterozygous. No polymorphism was found in rs11536865. Overall incidence of EAD was 27.5%(11/40). No difference between C/T($n = 9$) and non C/T ($n = 31$) rs913930 genotype pts was found in terms of median MELD, TIT, WIT, donor age, steatosis and proportion of urgent LTs. EAD occurred in 5/9 C/T and 6/31 non C/T rs913930 genotype pts ($p = 0.03$). Univariate regression analysis showed OR of EAD in C/T genotype of rs913930 equal to 5.2:1 ($p = 0.044$; 95% CI = 1–26.8). Limitation of the study is the number of observations at the time.
Conclusion: Polymorphism of TLR-4 gene in SNP rs913930 is probably implemented in EAD occurrence after DBD liver transplantation in Eastern European patients.

BO18 ASSOCIATION OF HLA-DQ POLYMORPHISMS WITH TRANSPLANT ETIOLOGIES AND LIVER FUNCTION RECOVERY IN LIVER TRANSPLANT RECIPIENTS

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Objectives: Recently genome wide association study showed that the genetic variants of human leukocyte antigen (HLA)-DP/DQ loci were strongly associated with a risk of hepatitis B virus (HBV) infection. The aim of this study was to investigate whether the HLA-DP/DQ loci was associated with liver transplant aetiologies and the liver function recovery in Chinese liver transplant recipients.
Methods: A total of 243 liver transplant recipients were enrolled into this study. The aetiologies of all those recipients were liver Cirrhosis (LC), hepatocellular Carcinoma (HCC), progressive HBV hepatitis and non-HBV related disease (including alcoholic hepatitis,hepatitis C or hepatic echinococcosis). Three single nucleotide polymorphisms (SNPs) HLA-DP (rs3077 and rs9277535) and HLA-DQ (rs7453920) were studied in all recipients by high-resolution melting (HRM) curve analysis. We dynamically detected the liver functions (including liver enzyme and coagulation index) before and after transplant.
Results: We found that the protective A allele of HLA-DQ (rs7453920) in LC (A = 4.4%) and HCC (A = 6.25%) recipients was much lower than non-HBV relative recipients (A = 16.7%). In addition, the direct bilirubin levels were lower in AG and AA genotype than those with GG genotyp before and after transplant, especially on the 14th day after surgery (17.80 vs. 5.35, p = 0.038, Figure 1). No significant correlation was found in HLA-DP (rs3077 and rs9277535) with HBV infection and liver function recovery.
Conclusions: HLA-DQ (rs7453920) was associated with transplant aetiologies as well as prognosis after liver transplantation. The A allele of rs7453920 served as a protective character in both HBV infection and liver function recovery after liver transplant.

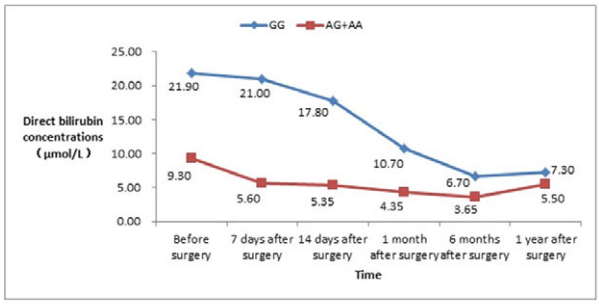

Figure 1. The association between the HLA-DQ rs7453920 and recipients' dynamic direct bilirubin concentration

BO19 ASSESSMENT OF LIVER STIFFNESS BY SHEAR WAVE ELASTOGRAPHY IN LIVER TRANSPLANT RECIPIENTS

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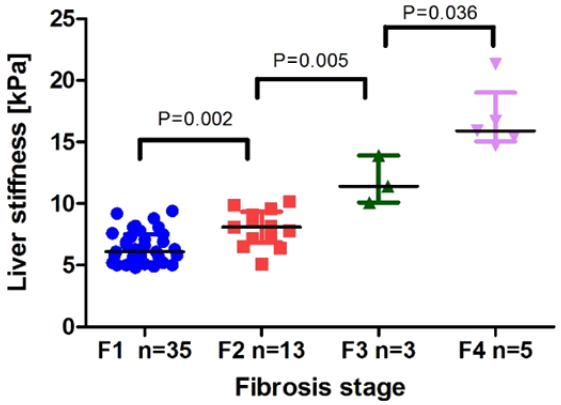
Background: Shear wave elastography (SWE) is a progressive method for non-invasive assessment of liver fibrosis. SWE results should be validated according to biopsy-proven stage of liver fibrosis to be applicable in clinical practice. The number of validation data, especially in hepatitis B and C, is increasing. Validation data concerning fibrosis in the liver transplant recipients are still missing. The aim of the study was to correlate SWE-assessed liver stiffness using Aixplorer ultrasound imaging system and biopsy-proven fibrosis of the liver graft.
Methods: Fifty-six consecutive patients (29 males and 27 females, median age 58 years, median follow-up from transplantation 61 months) with an inflammatory injury of the liver graft (recurrent hepatitis B and C, autoimmune hepatitis and allograft hepatitis) underwent protocol biopsy of the liver graft and SWE on the same day. Patients with recurrence of cholestatic liver diseases and patients with severe steatosis of the graft were excluded. Fibrosis stage was evaluated by one pathologist using the following semi-quantitative score: F1-portal fibrosis without septa, F2-portal fibrosis with few septa, F3-septal fibrosis, F4-cirrhosis. Liver stiffness was calculated as mean value of 3 different areas measurements of the liver graft.
Results: Results are shown in the figure. A significant difference in SWE liver graft stiffness was found between the all subgroups according to biopsy-proven fibrosis stage. SWE has AUCs of 0.86, 0.99 and 1.00 for F ≥ 2, F ≥ 3 and F = 4, respectively.



Conclusion: SWE may represent a simple and non-invasive method for assessment of liver graft fibrosis, but further validations for different types of liver graft injuries are needed.

BO20 EARLY LIVER ALLOGRAFT DISFUNCTION: RISK FACTORS AND OUTCOMES

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Background: Early liver allograft dysfunction (EAD) is associated with high incidence of graft loss and patient mortality. The aim of this study is to identify the risk factors of EAD and to compare the results in EAD and non-EAD groups.
Materials and Methods: The results of 213 consecutive deceased donor liver transplantations performed in our Center between December 2004 and February 2015 were included in the analysis. Indications for transplantation were non-viral liver cirrhosis – 52% (n = 111), viral hepatitis C or B – 34% (n = 72), then hepatocellular carcinoma – 8% (n = 17) and 6% (n = 13) of retransplantations due to previous liver graft dysfunction. Mean recipients age was 42 ± 13 years and mean MELD score – 18 ± 6. EAD was defined by Olthoff criteria (Olthoff et al., 2010).
Results: Overall incidence of EAD was 41.3% (n = 88), including 5.6% (n = 12) of primary non-function grafts (PNF), i.e. irreversible EAD. There were neither significant differences in donors' parameters (age, gender, cause of death, bilirubin, AST, ALT, sodium, macrovesicular steatosis) nor in recipients' (age, gender, diagnosis, body mass index, MELD) between EAD and non-EAD groups. Retransplantation, MELD score >30 and cold ischemia time (CIT) >8 h were independent significant risk factors of EAD in a multivariate model. In EAD group 30-day mortality rate was 18.2% (n = 16), mostly due to PNF without urgent retrasplantanion – 9.1% (n = 8), in non-EAD group – 0.0% (Fisher exact p 25 (n = 6) was 83%, in cases with MELD score ≤25 (n = 7) – 14%, Fisher exact p = 0.0291.
Conclusion: CIT using HTK solution is most important modifiable risk factor with optimal timeframe 4 – 6 h. Risk factors for irreversible EAD (PNF) were not yet defined. The advisability of late retransplantation in patients with MELD > 25 is controversial because of high incidence of PNF.

029 PANCREAS

BO21* THE ROLE OF NUTRITIONAL ASSESSMENT AND EARLY ENTERAL NUTRITION FOR SIMULTANEOUS PANCREAS KIDNEY TRANSPLANT CANDIDATES

Elijah Ablorsu, Dawn Chapman, Argiris Asderakis, Doruk Elker, Sally Finlay
Cardiff Transplant Unit

Introduction: Early post-operative enteral nutrition (EEN) is an important part of perioperative management and strongly supported by ESPEN Guidelines. However, there is limited evidence into the use of EEN after combined Pancreas-Kidney Transplantation (PKT). We know malnutrition in type-1 diabetics with end stage renal failure (ESRF) is a common problem and significant risk factor. Therefore, we introduced EEN in our patients.
Method: Compared 29 PKT recipients who underwent transplant between 10/2007 and 1/2010 without a nutritional assessment or planned EEN [Monitored Group (MG)] and compared to 30 PKT recipients transplanted between 2/2010 and 12/2013 who received nutritional assessment and EEN (NJ feed or oral intake with supplementation, according to their nutritional status) [Fed Group (FG)].The end-point was to assess patients' daily post-transplant nutritional intake. This was calculated as a percentage of estimated nutritional requirements using the Schofield equation with a 25% added stress factor and relevant activity factor. Realistic targets were to reach >60% nutritional of requirements by day-7 and at the time of discharge.
Results: There was no significant difference between MG and FG patients in CIT, recipient-age and donor-age, Length of Stay, donor-creatinine. In contrast, FG patient were less frequently in pre-dialysis status 41.4% vs. 26.7%, $p = 0.001$; and they had higher incidence of BMI <22.5 kg/m^2 63.3% vs. 0.48.3%, $p \leq 0.005$.In outcomes, FG patients more frequently achieved average % of nutritional requirements in first week 39.69% vs. 22.37%, $p \leq 0.005$; as well as during whole in-patient stay 57.24% vs. 44.43%, $p \leq 0.005$. The FG spent a greater proportion during first week, meeting more than 60% of nutritional requirements 66.7% vs. 31%, $p \leq 0.005$; as well as during whole admission 93.3% vs. 75.9%, $p \leq 0.005$. The need for parenteral nutrition within the FG was significantly lower, 7.1% vs. 20.7%, $p < 0.005$.

BO22 HOW USEFUL ARE THE US PDRI AND THE EUROPEAN P-PASS SCORES IN PREDICTING OUTCOMES IN UK PANCREAS TRANSPLANT PATIENTS?

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Cardiff Transplant Unit

Introduction: The US Pancreas Donor Risk Index (PDRI) and the European Preprocurement Pancreas Allocation Suitability (P-PASS) scores were designed to aid the decision-making process in accepting pancreas donor organs for transplantation. PDRI score ≥1.57 was associated with worse graft survival and P-PASS score <17 determined as the 'ideal' pancreas donor. The aim of this study was to determine whether these scores were associated with actual graft outcomes in pancreas transplantation.
Methods: The PDRI and P-PASS scores were retrospectively calculated from a prospectively maintained database for consecutive pancreas transplant recipients in a single centre. The patients were stratified according to type of transplant, and the PDRI and P-PASS scores were compared for correlation, graft survival and rejection episodes.
Results: Over a 10-year period, 119 pancreas transplants were performed in a single transplant centre, of which data was available for 115 to calculate the PDRI and P-PASS scores. Median PDRI and P-PASS scores were 1.93 (0.95–4.68) and 17 (10–23) respectively. Both the PDRI and P-PASS scores were significantly lower for PTA patients compared with PAK and SPK patients ($p < 0.05$).

The PDRI score correlated with the P-PASS score ($r^2 = 0.367$, $p < 0.0001$).

One-year graft survival was 94% and 85% for 'PDRI ≤1.57' and 'PDRI >1.57' groups respectively (log rank p-value of 0.332), and 91% and 86% for 'P-PASS <17' and 'P-PASS ≥17' groups respectively (log rank p-value of 0.824).

Thirty-three patients (29%) experienced at least one episode of rejection. Of these, 5 (14%) and 28 (37%) were in 'PDRI≤1.57' and 'PDRI >1.57' groups respectively ($p = 0.011$), and 11 (19%) and 22 (37%) in 'P-PASS <17' and 'P-PASS ≥17' groups respectively ($p = 0.032$).
Conclusion: Interestingly, this study shows that PDRI score ≤1.57 and P-PASS score <17 were associated with significantly fewer episodes of rejection. This may be a coincidental finding, and an analysis of a larger cohort is probably required.

Both scores were not able to predict actual graft survival outcomes from data available at the time of organ offer in this cohort of UK pancreas transplants. Development of a UK-specific score may allow for better prediction of graft survival outcomes.

BO23* BLADDER VERSUS ENTERIC DRAINAGE OF SOLITARY PANCREAS TRANSPLANTS: IS THERE AN ADVANTAGE?

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[1]Oxford Transplant Centre; [2]University of Oxford

Immunological monitoring of pancreas transplantation alone (PTA) has been challenging. Bladder drainage to monitor urinary amylase levels potentially offers a means to detect and treat rejection episodes early, and may reduce immunological graft loss.
Methods: A retrospective cohort study of enteric (ED) and bladder drained (BD) PTA was carried out at a single centre, where bladder drainage was systematically introduced in 2011. Primary end-point was pancreas allograft survival; secondary endpoints included renal dysfunction, hospital stay, readmission rate and enteric conversion.
Results: 108 PTAs (38 BD and 64 ED) were performed on 108 type 1 diabetics between 2006 and 2014. Median follow up was 14 months for BD-PTA and 38 months for ED-PTA. Mean donor age (35 ± 14 years vs. 34 ± 13 years), donor BMI (22 ± 3 vs. 23 ± 3), cold ischemia duration (666 ± 162 min vs. 694 ± 194 min), DCD grafts (24% vs. 34%), re-transplants (12% vs. 8%), recipient age (42.1 vs. 42.2), BMI (25.7 ± 3 vs. 24.6 ± 3.5), hospital stay (15.5 ± 7 days vs. 16 ± 14 days) was similar between BD & ED PTA. BD recipients had more frequent emergency re-admissions (median 3 vs. 1), mainly for dehydration, acidosis and urinary complications. 52% of BD recipients underwent enteric conversion at 11 months (range 3-26). Renal function at 1 y calculated by MDRD GFR declined significantly in BD (80 ± 28 ml/min to 63 ± 23 ml/min; $p = 0.0002$) in comparison to ED recipients (74 ± 32 ml/min to 64 ± 29 ml/min; $p = 0.22$). 15% of BD recipients received steroid therapy for suspected acute rejection due to a significant drop in urinary amylase/creatinine ratio. 1-year pancreas graft survival was 83% in BD-PTA vs. 74% in ED-PTA, ($p = 0.3$).

Discussion: Early results indicate potential advantage with better graft survival for bladder drained pancreas grafts, but also stress that the risks of metabolic and urinary complications should be carefully counseled pre-transplant.

BO24 PANCREAS ALLOGRAFT THROMBOSIS – REVISITING THE ROLE OF HYPERCOAGULABILITY

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Background: Pancreas allograft thrombosis continues to present a significant problem in the early post transplant period. The role of thromboelastography (TEG) directed anticoagulation and the effect on graft thrombosis is discussed.
Methods: All patients who underwent pancreas transplants at a single centre for 2013 were retrospectively analysed. Primary end point was the incidence of graft thrombosis, correlated with donor variables (pancreas donor risk index PDRI), preservation time, and recipient hypercoagulability as measured using the TEG.
Results: During 2013, 71 pancreas transplants were performed, with 57 SPK, 12 PTA and 2 PAK. During this period, 12 patients (17%) demonstrated evidence of thrombosis on CT / MRI angiography; seven patients had arterial thrombus (distal SMA), three patients the vein could not be demonstrated and presumed to have a thrombus, and three patients had both arterial and venous thrombosis. 1 graft (1.4%) was lost to thrombosis. 10 patients received therapeutic anticoagulation with low molecular weight heparin and have functioning grafts. Coagulation index >3 indicating hypercoagulability was associated with 9 thrombosis, whereas 3 occurred in patients with normal coagulation index. There was no correlation between donor age, BMI, cold ischaemia, donor PDRI, preop hypercoagulability and the occurrence of thromboses. Discussion: Graft thrombosis is multifactorial and the judicious use of anticoagulation directed by TEG as a tool to identify hypercoagulability improves the likelihood of graft salvage.

BO25 CONTRAST ENHANCED ULTRASONOGRAPHY IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION

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Introduction: Vascular complications following simultaneous pancreas and kidney transplantation (SPKT) remain the most common causes of peri-operative graft loss. Currently, investigative options are expensive, often

cumbersome, involve ionising radiation and potentially nephrotoxic contrast agents and therefore cannot be used for screening.

Contrast enhanced ultrasound (CEUS) combines conventional B-mode ultrasound with microbubble contrast technology, providing a safe, cheap, reiterative and bed-side imaging modality to assess potential complications following SPKT.

This study aimed to evaluate the feasibility of conducting CEUS in the peri-operative period following SPKT and assesses the potential benefits of the technique in this cohort of patients.

Methods: CEUS was carried out on the Intensive Care Unit by a dedicated transplant radiology team within 72 h post-SPKT. SonoVue was the contrast agent of choice.

Results: 12 SPKT recipients were recruited to the study (10 male (83.3%), mean age 39.33 (SD 8.917) and mean BMI 25.99 (SD 3.14)).

Primarily, CEUS was found to aid in the identification of pancreatic allograft vasculature and morphology when compared to standard B-mode and duplex US.

In addition, mean time from injection of, to visualisation of contrast within pancreatic parenchyma was 29.68s (SD 8.68s) and significantly correlated to serum amylase (145.5 mmol/l (IQR 99.75- 309.5), $p = 0.019$ and $r = 0.799$, Spearman Correlation) on the day of imaging.

There were no adverse effects of using Sonovue contrast agent in this cohort.

Conclusions: CEUS is a feasible and potentially useful adjunct in the peri-operative assessment of allograft perfusion and morphology following SPKT and may negate the need for CT angiography. It appears to have utility in identifying acute inflammatory processes within the allograft pancreas.

BO26 WHICH PLACE FOR PANCREAS GRAFT BIOPSY IN THE MANAGEMENT OF PANCREAS TRANSPLANT RECIPIENTS?

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Hospices Civils de Lyon

Introduction: Rejection or autoimmune recurrence is often difficult to diagnose in the field of pancreas transplantation. The place of pancreas graft biopsy in the management of pancreas transplant recipients is poorly defined. The aim of this study was to assess the contribution of pancreas graft biopsy in our cohort.

Methods: All recipients of pancreas transplant, who had a pancreas graft biopsy for cause since 2011, were included. Biopsies were performed under ultrasound or computer tomographic guidance and were graded according to Banff classification. We analyzed indications, results, concordance with kidney graft biopsies, and complications.

Results: Thirty pancreas biopsies were performed in 25 patients. Seven (23%) were non adequate. Twenty-five biopsies were performed for suspicion of rejection (increase in serum lipase $n = 19$, de novo DSA $n = 3$, kidney graft rejection $n = 3$). Among them, 15 showed rejection (grade I ($n = 8$) and grade II ($n = 6$) cell-mediated rejection, antibody-mediated rejection $n = 1$); 2 were indeterminate and only 2 were normal (6 non adequate). Evolution after treatment was favorable for all patients with grade I rejection. However, 5 out of 6 patients with grade II rejection lost their graft within 6 months. Biopsies performed for abnormal OGTT ($n = 2$) showed no rejection or abnormal islets. Biopsies for hyperglycemia ($n = 2$) were probably too late (1 grade II cell-mediated rejection, 1 non adequate) with adverse evolution. Biopsy for unexplained inflammatory syndrome was normal. Concordance of pancreas biopsy with kidney biopsy in patients having a kidney graft from the same donor was poor (3 of 9). There were no complications of biopsies.

Conclusion: Pancreas graft biopsy is essential for the diagnosis and prognosis of pancreas rejection and must be performed in every case of increase in serum lipase or de novo DSA. Concordance with kidney biopsy is poor. The place of pancreas biopsy in autoimmune recurrence still has to be evaluated.

BO27* LIRAGLUTIDE IN PANCREAS TRANSPLANT PATIENTS WITH IMPAIRED GLUCOSE HOMOEOSTASIS

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Hyperglycemia and diabetes may develop after months or years following whole-pancreas transplantation (PTX) among type 1 diabetes mellitus (T1DM) transplant recipients. Causes of chronic pancreas endocrine dysfunction are numerous including immune (allo and auto-reactions) and non immune reasons (drug toxicity, ischemia-reperfusion lesions, viral). Several medical attemps can be proposed to ameliorate this metabolic condition: CNI and steroid withdrawal, anti-diabetic oral agents, insulin. The efficacy and tolerability of GLP-1 receptor agonists have not been assessed in this population. We report here a 6-month prospective follow-up of six T1DM recipients of PTX (mean time after PTX, 68.8 $\pm$ 45.7 months), all of whom had an HbA1c>6.5% (48 mmol/mol) [mean: 7.1% (54 mmol/mol)] after initiation of liraglutide alone at 0.6 mg once daily titrated to 1.2 mg once daily at week 1. Gastrointestinal disorders were reported in three of the six patients, with discontinuation of liraglutide in only one patient. HbA1c improved in the five remaining patients, with a median decrease of 0.8% (0.0-2.7%) at 6 months, and the median decrease in body weight was 2.0 kg. Immunosuppressive treatment remained unchanged under liraglutide treatment (CNI was not interrupted). Liraglutide appears to be an effective and well-tolerated option in PTX patients with impaired glucose homoeostasis after several months of pancreas transplantation, regardless of the cause.

BO28 HIGH INSULIN RESISTANCE INDEX IN PANCREAS-KIDNEY TRANSPLANTATION IS ASSOCIATED WITH WORST PANCREAS-GRAFT'S SURVIVAL

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Background: Pancreas-kidney transplantation (PKT) is the best therapeutic option for end-stage renal failure due to diabetes. Peripheral insulin resistance and percentage of remaining beta cells in the PKT have not been sufficiently studied in the medical literature. The aim of this study was to analyze the glycemic profile and the influence of the peripheral insulin resistance in the pancreas graft survival.

Methods: We analyzed PKT performed in our hospital from January 1992 to January 2014, with follow-up for 5 years. Metabolic values related to glycemic were studied: proteinuria, peptideC, glucose, insulin and glycosylated hemoglobin. We analyzed the insulin resistance (HOMA-IR), the percentage of remaining beta cells (HOMA-beta) and the influence of these on the glycemic profile and graft survival.

Results: 156 simultaneous PKT were performed in our center. At 2 years after transplantation, the median value of HOMA-IR post-transplantation kidney-pancreas was 4. We compared transplantation with lower HOMA-IR (HOMA-IR<4) and higher (HOMA-IR>4). HOMA-beta, glucose and body mass index (BMI) were more elevated in group HOMA-IR>4 versus HOMA-IR<4 group (36(26–67) vs. 29(14–42)%, $p = 0.04$; 86 (80–90) vs. 81(74–89), $p = 0.018$; 24(21–27) vs. 21(19–24), $p = 0.013$) respectively after 3 months.These differences in glycemic profile were maintained until the first year after transplantation. At 2 and 5 years of follow-up, HOMA-IR>4 group showed higher glucose and BMI but not showed differences in HOMA-beta. At 1 and 5 years post-transplantation, pancreatic graft survival in HOMA-IR >4 group was lower compared to group HOMA-IR <4, being 82.9% versus 92.5% and 67% vs. 87.5% ($p = 0.016$) respectively.

Conclusions: Pancreas-kidney transplantation exhibit an altered glycemic profile in the post-transplantation follow-up associated with the percentage of remaining beta cells and peripheral insulin resistance. Pancreas-kidney transplant patients with peripheral insulin resistance showed decreased pancreatic graft survival.

BO29 IMMUNOLOGIC REJECTION OF A METASTATIC DONOR-DERIVED BELLINI DUCT CARCINOMA IN A KIDNEY TRANSPLANT RECIPIENT

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Introduction: Bellini duct carcinoma is a rare and aggressive tumor of the kidney originating from collecting duct cells, and has a poor prognosis with a median survival <11 months.

Methods: We report the case of 50-year-old woman who received kidney-pancreas transplantation for type I diabetes and who developed a metastatic donor-derived Bellini duct carcinoma with metastatic implants in the peritoneal cavity, small and large bowel, liver and lungs 9 years after transplantation.

Results: The kidney graft was removed and the metastases were confirmed by histological analysis. XY karyotype was demonstrated by FISH in tumor cells confirming the donor's origin of the tumor. To induce a strong host versus graft/tumor response, the kidney graft was removed, immunosuppression was withdrawn, and rIL-2 was administered at 6 MIU for 3 months. The patient returned to dialysis and insulin therapy. Three months after discontinuation of the immunosuppression, she developed pseudoaneurysm at the site of pancreas arterial anastomosis site that required surgical closure. No pancreatic tissue was found during the operation. Importantly, peritoneal, liver and lung metastatic lesions regressed at 3 months PET/CT control and no signs of recurrence were observed after 1 year of follow-up. Absolute number of circulating T and NK cells increased, which is compatible with a strong lymphocyte proliferation following rIL-2 therapy. The CD4+/CD8+ T cells ratio decreased from 80% to 50%. HLA-DR expression on T cells significantly

increased from 6% to 44%. The cytokine profile showed increased level of IL-2 and IFN-γ. No anti-HLA antibodies were detected. However no specific anti-donor antibodies were identified.
Conclusion: This case suggests that a vigorous host immune response was able to reject a metastatic tumor of donor origin. Immunosuppression withdrawal and rIL-2 treatment was associated with a cell-mediated immunity response that involved NK and CD8+ T cell against tumor expantion.

BO30* CHANGES IN BONE MINERAL DENSITY FOLLOWING LONG TERM SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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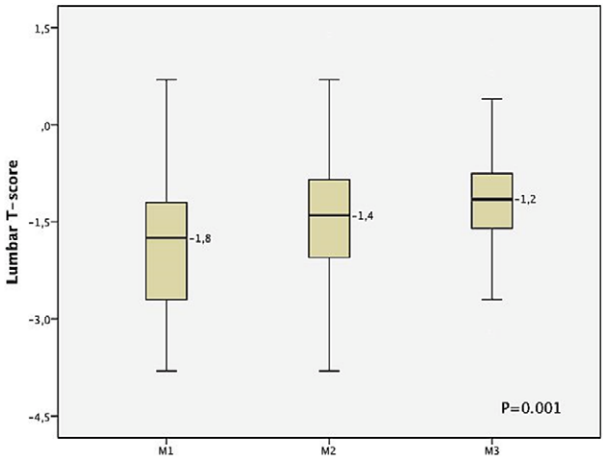
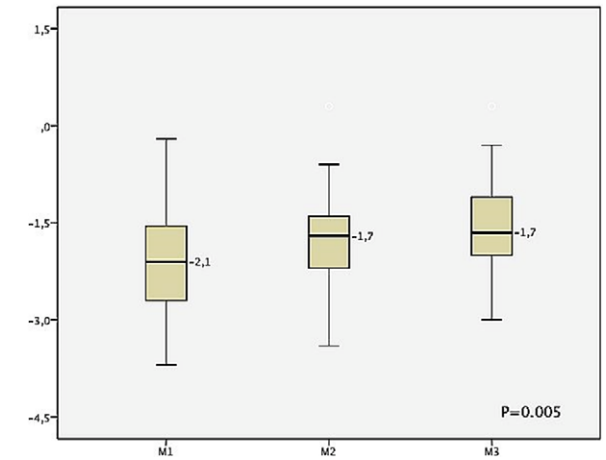
Purpose: The symptoms of renal osteodystrophy improve significantly in patients after successful simultaneous pancreas-kidney transplantation (SPKT); however bone pathology is still present even after many post-transplant years. The aim of this study was to analyze the bone densitometry in different periods after SPKT.
Methods: Three-point densitometry was performed with dual-energy x-ray absorptiometry (DXA) technique. Serum levels of alkaline phosphatase (ALP), total serum calcium, phosphate and parathyroid hormone were analyzed as markers of mineral metabolism.
Results: Study population consisted of 48 patients of mean age 35 ± 6 years (28F, 20M) and mean 24 ± 6 years of prior diabetes. Mean period of maintenance dialysis was 36 ± 26 months. The median time from SPKT and DXA measurement was 0.53, 26.2 and 41.9 months, respectively. Based on DXA technique, 35.4% of patients were categorized as having osteoporosis at lumbar spine and 39.6% at femoral neck. Patients with diagnosed osteoporosis had significantly higher level of ALP (OR = 1.5; 95% CI = 1.1–2.2; $p < 0.05$ at lumbar spine; OR = 1.4; 95% CI = 1.0–1.9; $p < 0.05$ at femoral neck). In addition, subjects with lumbar osteoporosis were characterized by significantly lower body mass index (BMI) (OR = 0.5; 95% CI = 0.3–0.9; $p < 0.05$). In long-term follow-up, BMD increased significantly at lumbar spine and femoral neck. Multivariate linear model identified BMI increase as a significant factor associated with improvement in BMD.





Conclusions: Results of our study led us to conclude that BMD in three-point densitometry among patients with functioning kidney and pancreas graft improved. Increased serum levels of ALP associated significantly with a decrease of BMD suggesting a higher risk of osteoporosis. BMI gain was predictive of BMD improve.

013 IMMUNOBIOLOGY/BASIC SCIENCE

BO31 OXIDATIVE STRESS DURING ORGAN RETRIEVAL IMPACTS TRANSPLANT VASCULOPATHY DEVELOPMENT

Rupert Oberhuber[1], Gregor Riede[1], Benno Cardini[1], Bernhard David[2], Barbara Messner[3], Katrin Watschinger[4], Christina Steger[5], Gerald Brandacher[6], Johann Pratschke[7], Ernst Werner[4], Manuel Maglione[1]
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Transplant vasculopathy represents a major obstacle to long-term graft survival. Treatment strategies aiming at preventing it are still lacking. Herein we present that the occurrence of transplant vasculopathy crucially depends on oxidative stress formation during organ retrieval.A fully MHC mismatched (BALB/c to C57BL/6) mouse aortic transplantation model was used. Before organ recovery donor animals received either saline (group I–IV) or 50 mg/kg b.w. tetrahydrobiopterin i.m. (group V–VIII). Aortic grafts were analysed at 4 different time points: (a) immediately following recovery (group I + V), (b) following 24 h cold ischemia time (CIT; group II + VI), (c) following 24 h CIT and 45 min anastomosis time (group III + VII), (d) following 4 weeks graft reperfusion (group IV + VIII). Aortic tetrahydrobiopterin tissue levels were analysed by HPLC, oxidised proteins were measured by the Oxyblot procedure. Transplant vasculopathy was diagnosed by histopathology and immunohistochemistry. 24 h CIT and 45 min anastomosis time resulted in strong neointima formation and α-smooth muscle actin expression, which could be prevented by donor pre-treatment with tetrahydrobiopterin ($p = 0.008$ and $p = 0.01$, respectively). Similarly, endothelial expression of P-selectin was significantly decreased in the pre-treatment group ($p = 0.01$). Interestingly, grafts from pre-treated donor mice showed significantly less oxidised proteins than non-treated grafts already at the time of organ retrieval and following 24 h CIT, but not at later time points ($p = 0.003$, $p = 0.02$ and p = ns, respectively).These data indicate an important role of oxidative stress already during organ recovery, initiating chronic inflammation, which then leads to chronic rejection. Analysing the protective mechanism of tetrahydrobiopterin might unravel strategies to minimise transplant vasculopathy in solid organ transplantation.

BO32 RAPAMYCIN PROTECTS KIDNEY FROM ISCHEMIA REPERFUSION INJURY VIA MODULATING INNATE IMMUNE CELLS IN SITU

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Background: Rapamycin plays a protective role in kidney ischemia reperfusion (IR) injury in early stage, but the mechanism involved hasn't been thoroughly revealed. We investigated in this study the modulatory effects of rapamycin on dendritic cells (DCs), macrophages and NKT cells in spleen, peripheral blood and IR induced kidney in the murine model. The effect of rapamycin on multiple damage-promoting or damage-preventing immune molecules were also investigated.
Material and Methods: Balb/c mice were subjected to kidney 30 min ischemia followed by 24 h reperfusion. Rapamycin (2.5 ml/kg) was administered by gavage daily, starting 1 day before the operation. Renal function and histological changes were assessed. The proportion of NKT cells, macrophages and DCs in peripheral blood, spleen and kidney was detected. The expression of pro-inflammatory cytokines IL-6, MCP-1, TNF-α, IL-β1 and anti-inflammatory cytokines IL-10, TGF-β were determined by RT-PCR.
Results: Rapamycin improved renal function and ameliorated histological injury. In rapamycin-treated group, the proportion of NKT cells in spleen was significantly decreased but increased in peripheral blood and kidney. The proportion of macrophages in spleen was decreased in rapamycin group. In peripheral blood, there is no significant difference between each group. The proportion of macrophages was raised in rapamycin group. In spleen, rapamycin increased the proportion of dendritic cells, but the proportion was decreased in peripheral blood and kidney. In addition, rapamycin dramatically down-regulated the expression of IL-6, MCP-1, TNF-α and IL-β1 compared with IR group in which these pro-inflammatory cytokines was increased. The expression of IL-10 and TGF-β was markedly up-regulated after rapamycin administration.
Conclusions: Rapamycin may protect murine kidney from ischemia reperfusion injury through modulating immune cells and molecules.

BO33* MYELOID HEME OXYGENASE-1 CONTROLS RENAL ISCHEMIA-REPERFUSION INJURY

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Background: Renal ischemia reperfusion injury (IRI) leads to major organ and cell damages by at least the activation of innate immunity. The heme oxygenase-1 (HO-1), a stress-responsive enzyme, protects kidney from renal IRI through multiple mechanis. In kidneys, HO-1 can be expressed by many cellular sources among which tubular epithelial cells and myeloid cells. The aim of this study was to understand the role of the myeloid HO-1 in the natural control of renal IRI and after pharmacological induction of HO-1 by hemin.
Materials and Methods: Myeloid HO-1 KO mice (HO-$1^{M\text{-}KO}$ mice), specifically deficient for HO-1 in myeloid cells, littermate (LT) control mice, and wild-type (WT) C57/Bl6 mice underwent bilateral renal IRI for 26 min. After 24 h of reperfusion, plasma and kidneys were harvested. WT mice were treated with hemin 5 mg/kg or saline 24 h prior ischemia. Renal IRI was evaluated by plasma creatinine and histology. Renal inflammation, leukocytes influx and oxidative stress were assessed by ELISA, immunostaining and nitrotyrosine levels respectively. HO-1 expression in renal leukocytes was assessed by FACS.
Results: Renal damages were worsened in HO-$1^{M\text{-}KO}$ compared to LT mice (i.e. higher creatinine levels and tubular necrosis). Intrarenal cytokine expression (i.e. IL-6, MCP-1 and KC), oxidative stress and neutrophil/macrophage influx were also enhanced. In WT mice, the protective effect of hemin pretreatment (i.e. plasma creatinine levels, tubular necrosis) was associated with a specific upregulation of HO-1 within myeloid $CD11b^{+}F4/80^{lo}$ renal cells before IRI and a higher proportion of these HO-1 producing myeloid cells upon IRI. A subsequent dampened renal inflammation was found in hemin-treated mice (i.e. IL-6, MCP-1 and KC).
Conclusion: Our results demonstrate that myeloid-derived HO-1 in $CD11b^{+}F4/80^{lo}$ renal cells significantly controls the magnitude of renal IRI. Targeting myeloid HO-1 might represent a promising approach for preventing renal IRI.

BO34 URAEMIA INDUCES SKEWED T CELL RECEPTOR REPERTOIRES IN END STAGE RENAL DISEASE PATIENTS

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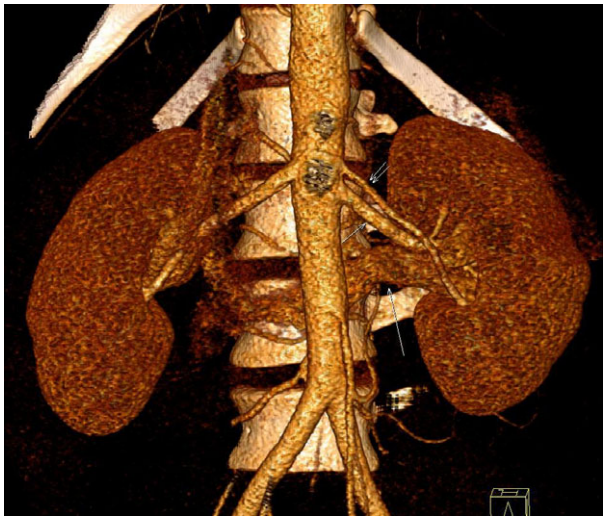
Erasmus MC

Background: A diverse T-cell receptor (TCR) repertoire is central to effective T-cell mediated immune responses. Little is known whether uraemia, associated with premature T-cell ageing, skews TCR repertoire diversity. This study aimed to assess the effects of uraemia on TCR repertoire diversity in ESRD patients and associate it with T-cell parameters.
Material/Methods: Fifty patients were recruited, divided into young (age<45 years) and old (age>65 years), compared to 51 age- and cytomegalovirus (CMV) serostatus-matched healthy individuals (HI). The TCR beta (TCRB) repertoire was evaluated by DNA-based multiplex TCRB gene PCR. The differentiation status and relative telomere length (RTL) of T cells were assessed by flow cytometry.
Results: Uraemia induced skewed TCR repertoires which was more pronounced ($p < 0.01$) amongst the elderly patients (84%) compared to their age-matched HI (32%). Only 44% of the young patients had a skewed TCR repertoire compared to 31% of the HI ($p > 0.05$). More CMV- seropositive patients had skewed TCR repertoires compared to CMV-seronegative patients (85% vs. 42%, $p < 0.01$). The elderly patients with skewed TCR repertoires had significantly less total, naive and more $CD28^{-}$ $CD4^{+}$ T cells compared to the elderly patients with unbiased TCR repertoires. In the young patients, skewed TCR repertoires were associated with more total, EMRA and $CD28^{-}$ $CD8^{+}$ T cells when compared to those with unbiased TCR repertories. The RTL of T cells was not significantly different between the patients with skewed and unbiased TCR repertories.
Conclusion: Uraemia skewed the TCRB repertoire in elderly ESRD patients and CMV latency added to this skewed TCRB repertoire. The skewed TCR repertoire is associated with more differentiated T cell subsets. Assessment of TCR repertoire diversity prior to kidney transplantation might contribute to proper risk assessment of allograft rejection.



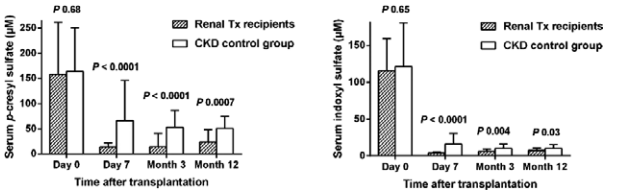
BO35

THE IMPACT OF RENAL TRANSPLANTATION ON MICROBIOTA DERIVED UREMIC RETENTION SOLUTES

Ruben Poesen, Pieter Evenepoel, Dirk Kuypers, Maarten Naesens, Björn Meijers

University Hospitals Leuven

Background: The gut microbial metabolism contributes substantially to uremic retention solutes accumulating in chronic kidney disease (CKD). Both p-cresyl sulfate and indoxyl sulfate are representatives of this group of solutes and associate with adverse outcomes in patients with renal dysfunction. Although it can be expected that serum levels of these microbial metabolites will decrease following renal transplantation, this has not been studied to date. In addition, whether serum levels of p-cresyl sulfate and indoxyl sulfate in renal transplant recipients are quantitatively different when compared to regular CKD patients is unknown.
Methods: A cohort of 51 CKD patients was prospectively followed from time of transplantation to 12 months post renal transplantation. Serum levels of p-cresyl sulfate and indoxyl sulfate were determined at time of transplantation, day 7, month 3 and 12 post transplantation. At each time point, serum levels of both solutes were compared with an unrelated group of CKD patients matched for age, gender, body mass index, presence of diabetes, dialysis modality/vintage at time of transplantion or renal function (serum creatinine, eGFR and measured creatinine clearance) at other time points, and biochemistry (hemoglobin, albumin).
Results: Serum levels of p-cresyl sulfate and indoxyl sulfate substantially decreased after renal transplantation ($p < 0.0001$ for both solutes at each time point versus time of transplantation). When compared to CKD control patients, serum levels of both solutes were still significantly lower in renal allograft recipients at each time point (see Figure 1). Additional analyses demonstrated lower urinary excretion rates of microbial metabolites in renal transplant patients ($p < 0.0001$).



Conclusions: Microbiota derived uremic retention solutes substantially decrease following renal transplantation. In addition, serum levels of these solutes are significantly lower when compared to regular CKD patients, suggesting an independent influence of renal transplantation or immunosuppressive drug therapy on the gut microbial metabolism. Whether these microbial metabolites are also associated with graft dysfunction and adverse outcomes in renal transplant recipients needs further investigation.

BO36

IMPAIRED IRON HOMEOSTASIS RESULTS IN ACCELERATED REJECTION AFTER EXPERIMENTAL HEART AND KIDNEY TRANSPLANTATION

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Background: Clinical data suggest that iron (Fe) overload deleteriously affects graft survival after heart (HTX) and kidney transplantation (KTX) but possible immunological mechanisms underlying this phenomenon have not been elucidated.
Methods: To identify the mechanistic influence of Fe in a murine model of HTX or KTX, fully allogeneic Balb/C donor organs were transplanted into Fe overloaded C57BL/6 recipients.
Results: Following HTX, Fe overload accelerated acute and chronic rejection as observed by a shortened graft survival (acute: HTX vs. HTX+Fe; $p < 0.05$; chronic: HTX vs. HTX+Fe; $p < 0.01$) and elevated ISHLT-rejection score ($p < 0.01$). FACS analysis revealed that in contrast to a pronounced graft infiltration of $CD4^+$ T ($p < 0.01$) and $CD3^-NKp46^+$ NK cells ($p < 0.05$), reduced frequencies of regulatory T cells (T_{Reg}) were detected in the graft and spleen ($p < 0.01$, respectively) derived from Fe overloaded recipients. This was accompanied by lower intragraft and splenic mRNA expression levels of anti-inflammatory cytokines (IL-10, TGF-beta) and Foxp3. Following KTX, analogous observations were retrieved analyzing NK cells, $CD4^+$ and T_{Reg} cells and expression profiles. Whereas transplantation per se activated splenic NK cells, this was further accentuated following Fe overload ($p < 0.01$). Interestingly, intra-graft induction of hepcidin and diminished CD71 expression ($p < 0.05$, respectively) suggest that the allograft itself - initially derived from a healthy donor - is affected by the Fe overload of the recipient.
Conclusion: Based on our data we provide novel insights into the understanding of disturbances in Fe homeostasis and their consequences following transplantation suggesting new perspectives for personalized immunosuppression in the future.

BO37

MITOCHONDRIAL FEEDBACK IS A KEY FEATURE OF KIDNEY GRAFT SENESCENCE

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[1]UZ Leuven; [2]U Hasselt

Background: Progressive DNA damage is considered one of the key instigators of ageing. Different models for ageing where DNA damage leads to accelerated senescence have been proposed.
Methods: A test cohort of 40 consecutive kidney donors, with pre-implantation renal allograft biopsies, was included in this study. Intrarenal and donor leucocyte telomere length, and mitochondrial DNA content was assessed using quantitative RT-PCR. In these same samples ($N = 40$), whole genome microarray mRNA expression analysis was performed using Affymetrix Gene 2.0 ST arrays ($N = 40$). The associations between mRNA gene expression and the biomarkers of replicative senescence were investigated using multiple regression models, adjusted for calendar age, gender and batch number. For biological interpretation, Ingenuity Pathway Analysis and Consensus software were used to identify overrepresented pathways. An independent cohort of 160 implantation biopsies was used for validation.
Results: In total, 1180 transcripts significantly associated with intrarenal telomere length, of which 611 were significantly upregulated with shorter telomeres. Pathway analysis revealed enrichment of transcripts coding for proteins of the citric acid cycle ($q = 1.06 \times 10–13$), transcripts involved in respiratory electron transport ($q = 1.06 \times 10–13$) and transcripts involved in oxidative phosphorylation ($q = 4.48 \times 0–10$). Also mitochondrial DNA content correlated highly significantly with telomere length ($r = 0.3$; $p = 0.0005$). Independent replication of these findings is on-going on a separate cohort of 160 pre-implantation biopsies.
Conclusion: This unbiased study suggests that mitochondrial alterations (DNA content and mitochondrial gene expression) are key features of replicative senescence of human kidneys. Upregulation of mitochondrial gene expression in baseline kidneys for transplantation is a protective feedback mechanism and a potential therapeutic target for improving renal allograft viability in the perioperative fase.

BO38 DYSREGULATION OF THE CHOLESTEROL PATHWAY ASSOCIATES WITH ARTERIOSCLEROSIS AND INTRARENAL TELOMERE ATTRITION

Katrien De Vusser[1], Kevin Hochstenbach[2], Ellen Winckelmans[2], Evelyne Lerut[1], Dirk Kuypers[1], Tim Nawrot[2], Maarten Naesens[1]
[1]UZ Leuven; [2]U Hasselt

Background: We demonstrated that arteriosclerosis in the smaller intrarenal arteries is associated with shorter telomere length, independent of cardiovascular risk factors and calendar age. The underlying mechanisms of this association remain unclear.
Methods: A test cohort of 40 consecutive kidney donors, with pre-implantation renal allograft biopsies, was included in this study. All biopsies were rescored according to the Banff classification. Intrarenal donor telomere length content was assessed using quantitative RT-PCR. In these same samples, whole genome microarray mRNA expression analysis was performed using Affymetrix Gene 2.0 ST arrays. The associations between mRNA gene expression, telomere length as marker of replicative senescence, and intrarenal arteriosclerosis were investigated using multiple regression models, adjusted for calendar age, gender and batch number. For biological interpretation and pathway overrepresentation analysis, Ingenuity Pathway Analysis software was used. An second cohort of 160 implantation biopsies was used for independent validation.
Results: Shorter intrarenal telomere length associated significantly with the presence of renal arteriosclerosis ($p = 0.007$). Pathway analysis revealed enrichment of transcripts coding for proteins of the superpatway of cholesterol biosynthesis as the most significant in the telomere attrition- arteriosclerosis model ($q = 0.0003$; $q = 2.69.10$ -8). The 10 most significant pathways in the model are all involved in cholesterol metabolism. These pathways are upregulated in the presence of arteriosclerosis and in case of shorter telomere length.
Introduction: Arteriosclerosis in smaller intrarenal arteries is independently associated with shorter telomere length. Our unbiased suggests that the pathways involved in the cholesterol metabolism are the missing link between the appearance of arteriosclerosis and telomere attrition. Validation of these findings is underway, in a cohort of 160 independant implantation biopsies.

BO39 AGED DONOR-DERIVED PASSENGER LEUKOCYTES DISPLAY AN INFLAMMATORY PROFILE

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Advanced donor age has been identified as an independent risk factor for the development of chronic rejection. Only limited data exist about the immune system in the elderly and little is known about the immunological phenotype of aged organs containing passenger leukocytes (DPLs). We therefore compared tissue-resident lymphocytes derived from solid organs and secondary lymphoid organs between young (8–12 weeks) and aged (18–20 months) C57BL/6 mice in a phenotypic and functional analysis. In general, donor age is associated with significantly higher numbers of DPLs in solid organs but not in secondary lymphoid organs. Moreover, aged organs are characterized by an increase of CD8+ central memory (TCM) and effector memory T (TEM) cells, whereas naïve T cells were significantly reduced. In contrast with CD4+ CD28− T cells, mainly tissue-resident CD8+ CD28− T-cells increase with age. We further detected comparable frequencies of CD3+ CD4+ CD25+ FOXP3+ TReg in young and elderly mice in solid organs and spleen, whereas numbers of CD8+ CD122+ TReg lymphocytes are significantly increased in secondary lymphoid organs but not in liver or kidney. Surprisingly, NKp46+ NK cells are decreased in both aged solid and lymphoid organs, but especially organ derived NK cells display a higher MHC class II expression. NKG2D, an activating receptor mainly found on NK cells and CD8+ T cells, is significantly upregulated on aged CD8+ T cells but not on NK cells suggesting this receptor as a novel senescence marker for CD8+ T cells. Furthermore, CD8+ NKG2D+ T cells derived from solid organs produce more granzyme B and perforin than derived from spleen. We demonstrate that the phenotype of aged tissue-resident lymphocytes is not mirrored by their counterparts in secondary lymphoid organs as these cells are characterized by a certain central and memory effector profile associated with higher cytotoxicity. Our data shed new light into the immunological status of solid organs derived from the elderly.

BO40 OBESITY ACCELERATES ALLOIMMUNITY AND REJECTION RATES WHILE BARIATRIC SURGERY PROLONGS GRAFT SURVIVAL

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Division of Transplant Surgery/Transplant Surgery Research Laboratory, Brigham and Women's Hospital

Background: Obesity has been conceptualized as chronic inflammatory condition, but little is known on its impact on immune responses. We hypothesized that (I) obesity will accelerate allograft rejection linked to pro-inflammatory immune responses and that (II) bariatric surgery will reverse the detrimental impact of obesity.
Methods: Skin transplantation was performed in diet-induced obese (DIO) C57Bl/6 mice and lean littermates utilizing fully MHC mismatched donors (DBA/2→C57Bl/6). In addition, sleeve gastrectomies (SGx) were performed in DIO mice to test effects on alloimmunity and transplant survival subsequent to a 2-week interval at which time weight loss had stabilized; systemic immune responses were tested serially ($n = 5$/group).
Results: Skin allografts are rejected significantly earlier in obese animals compared to lean controls (median graft survival 7 vs. 9 days). Of note, animals following weight loss surgery showed a significantly prolonged allograft survival (11 days; $n = 5$/group; Log-rank test: $p = 0.006$; Fig. 1). In addition, alloreactivity assessed by ELISPOT analysis was significantly reduced following SGx ($n = 6$/group by POD 6; $p < 0.05$). Detailed immune analysis subsequent to transplantation revealed a significant increase in IFN-γ production of splenic CD4+ T cells from obese animals; in contrast, animals following SGx showed I) a dramatic decrease in IFN-γ production and II) a significantly increased IL-10 production following transplantation ($n = 6$/group by POD 6; $p < 0.05$; Fig. 2).
Conclusions: Obesity is resulting in accelerated allograft rejection by promoting pro-inflammatory Th1-dominated conditions. In contrast, bariatric surgery prolongs graft survival beyond that observed in obese and lean animals by driving the alloimmune response towards protective Th2-dominated conditions.

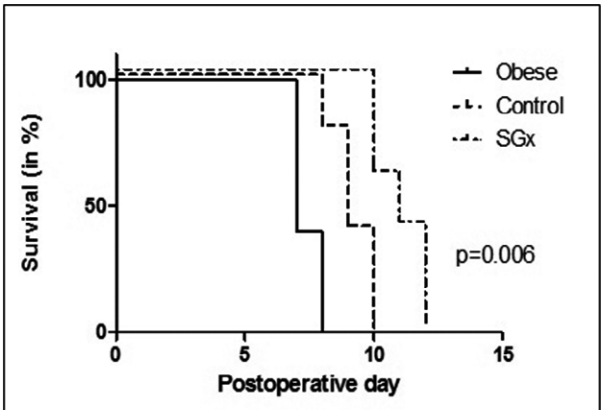

Fig. 1: Survival curve for allograft survival comparing obese vs. lean vs. sleeve gastrectomies (SGx) (log-rank: p=0.006)

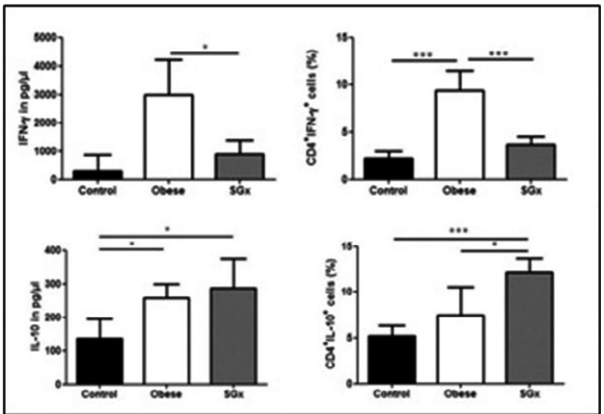

Fig. 2: Analysis of splenic CD4+ cells following transplantation by ELISA and FACS in obese, lean and recipients that underwent weight loss surgery (SGx) (*,p<0.05;***, p<0.001)

009 ETHICS/LAW/PSYCHOSOCIAL/PUBLIC POLICY

BO41 INFORMED CONSENT PROCESS SEEN BY KIDNEY TRANSPLANT RECIPIENTS IN A URUGUAYAN TRANSPLANT CENTRE

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Informed consent is a legal pre requisite to get into transplantation's waiting list and a second informed consent is also required for the transplantation procedure. Since kidney transplantation is a treatment that has to be requested by the patient willing to receive the graft, we could assume that in this particular setting the informed consent process should be easier. The aim of this study is to evaluate the process of informed consent from the patient view, either the ones in waiting list or the ones already transplanted.
Methods: We ask verbal consent prior telephone survey. From 817 transplanted patients we randomly selected 500 to survey. We aimed to survey all patients in the waiting list.
Results: From 1519 kidney transplant patients in the Nephrology and Urology Institute, 817 have a functioning graft; we evaluated 500 with an average age of 51 years (18–88), 195 (39%) female and 305 (61%) male. In 448 (89.6%) their nephrologists prompted to go to the waiting list, 39(7.8%) for personal inquiries and in 13 cases (2.6%) from other patient recommendation.

When asked about informed consent 245 (49%) recall having read, from this 203 (40.6%) remember having understood. We crossed having read the informed consent with age range, marital status, time since transplantation, educational level.

From 242 patients in waiting list, 48 didn't answer, 6 were transplanted, 3 were under 18 years, 15 had exclusion criteria and 2 died. From the 168 evaluated with an average age of 54 years (20–79), 51 (30.4%) female and 117 (69.6%) male. In 132 (78.5%) their nephrologists prompted to go to the waiting list, 18 (10.7%) for personal inquiries, in 8 (4,8%) from other patient recommendation and in 9(5.4%) all three.

When asked about informed consent 167 (99.4%) recall having read, from this 124 (73.8%) remember having understood.
Conclusion: Despite our prior belief the informed consent process should be modified on patients seeking kidney transplantation in Uruguay.

BO42 A LESSON ABOUT ORGAN DONATION IN PRIMARY SCHOOL: SUPPORT FOR ITS DEVELOPMENT AND ITS EFFECTS

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Background: Organ and tissue donation can also involve children. Because of its sensitivity, this topic requires careful decision making. Children, starting at a certain age, are capable of thinking about this subject and enjoy participating in family discussions about it. Therefore, what children need is proper information.
Purpose: When schools are used to educate children about this subject, information about teacher support for this type of lesson along with its effects on the depth of family discussions is important.
Methods: A questionnaire was sent to all 7542 primary schools in the Netherlands. The goal was to gather information on teachers' perspectives about a neutral lesson devoted to organ and tissue donation, and also on the best age to start giving such a lesson. Part B examined the effects of a newly developed lesson among 269 primary school pupils.
Results: Response 23%. Of these, 70% were positive towards a lesson; best age to start was 10-11 years. Part B, pupils reported 20% more family discussions after school education and enjoyed learning more about this topic.
Conclusion: There is significant support in primary schools for a school lesson on organ and tissue donation. Educational programs in schools support family discussions.

BO43 INCREASE IN THE RATE OF KNOWN WILL REGARDING ORGAN DONATION AFTER THE CHANGE OF THE TRANSPLANT LAW IN GERMANY

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Background: In Germany the existing informed consent was modified when the transplant law was revised in 2012. The insurance companies are now obliged to send out information about organ donation to every insured person ≥16 years every 2 years in order to stimulate decision making regarding organ donation. The aim of this study was to investigate whether this new policy had an effect on the rate of organ donation decisions that were based on the known will of the donor.
Methods: We evaluated the results of all donor family interviews reported to the German organ procurement organization (DSO) from 2009 to 2014; in the years 2012–2013 the insurance companies had for the first time sent out information based on the new law. The results were statistically analyzed and classified into three categories: known will (oral or written, $n = 4010$), presumed will ($n = 4780$) and decision made by donor families ($n = 2997$). Significance assumed if $p < 0.05$.
Results: Decisions regarding organ donation based on the known will increased from 30.6% in 2009 to 39.4% in 2014. At the same time decisions based on a presumed will declined from 43.3% in 2009 to 35.5% in 2014 ($p < 0.001$). This shift was most pronounced in cases with consent to donation ($n = 7246$): known consent 29.9%→ 42.1%; presumed consent 52.1%→ 40.9% ($p < 0.001$) compared with refusals ($n = 4741$): known refusal 31.8%→ 35.4%; presumed refusal 29.3%→ 27.3% ($p = 0.249$). The percentage of the decisions made by donor relatives, without knowing the will of the deceased one, was not statistically different.
Conclusion: The obligatory information of every insured person regarding organ donation seems to have a positive effect on the percentage of declared intentions towards organ donation. This increase of donors with a known will may reduce the known burden of the relatives when confronted with the request for organ donation.

BO44 BEHAVIOR MODIFICATION MECHANISMS FOSTERING THE INTENTION TO DONATE ORGANS: AN EMPIRICAL STUDY OF 10 000 CASES

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Doshisha University

Background: It has been reported that of families consenting to organ donation following brain death, 90% did so to respect the wishes of the donor. Similarly, in a 2013 opinion poll, 87% said they would respect the wishes of someone who had expressed in writing their intention to donate. This suggests the importance of individual expression of the desire to be a donor. Yet only 12.6% of Japanese people have done so. This study elucidated the mechanisms by which the general public can express their intention to be a donor and clarified the interventions needed for them to do so.
Methods: A web questionnaire was completed by 10 000 Japanese individuals aged 20 years and over. Data were analyzed using factor analysis, *t*-tests, and logistic regression.
Results: Of the sample, 43.4% were interested in organ donation, and of these, 85.4% intended to express their interest; 52.3% of these had actually done so. Thus, interventions are needed in "having the person become interested" and "transitioning an attitude to behavior." Regarding the former, analyses showed the utility of promoting models of assistance, empathy, and altruistic behavior via the media, and providing correct information on transplants and organ donation. Regarding the latter, analyses showed the effectiveness of eradicating anxiety about organ donation by having potential donors interact with actual donors. Such interventions increase recognition that trustworthy people are donors and increase individual convictions to express their intention (i.e., self-efficacy), transitioning to actual behaviors.
Conclusion: It was clarified that different interventions are required for different behavioral stages. The findings suggested the importance of ascertaining the behavior modification stage of each person and to carry out appropriate interventions, so that attitudes become actual behaviors.

BO45 TRAFFICKING IN HUMAN BEINGS FOR THE PURPOSE OF ORGAN REMOVAL: A COMPREHENSIVE LITERATURE REVIEW

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Background: In 2012 the European Commission funded 'The HOTT Project': an international research project against trafficking in human beings for the purpose of organ removal (THBOR), that aims to generate knowledge and awareness about the crime. The project's first report, a large-scale literature review, fulfils this objective by describing existing information on the scale and true nature of THBOR and by identifying literature gaps.
Methods: We performed literature searches in EbscoHost, Library of Congress Catalog, OAIster, PubMed, Scopus, EthxWeb, GoogleScholar,

Web of Science, Medline OvidSP and Cochrane. The searches were based on key words. Priority was given to scientific works that present data based on qualitative and/or quantitative study methods.
Results: The report presents the actors in the THBOR network. Brokers contribute most to the exploitation of suppliers by deception, force and coercion; however, many details concerning practicalities remain unclear. Suppliers are the victims - being recruited, transported, harbored and/or received by facilitators, brokers, recipients, doctors who abuse their vulnerability. Suppliers receive low pay for their organ, or nothing at all. Recipients travel abroad for transplantation and pay for organ transplants. The most popular destinations are China, Pakistan and India. The literature is inconclusive about whether these patients receive their organs through THBOR. Transplant professionals are involved in illegal transplant operations, but it is unknown whether they have been prosecuted. Other facilitators of THBOR are hospitals, service providers, translators and corrupt law enforcement officials.
Conclusion: We conclude that the existing literature is insufficient in providing information about the scale and true nature of THBOR. Empirical fieldwork seems to be a more appropriate source to gather information about the phenomenon and the role, modes of operation and degree of organization of the actors involved.

BO46* ONE DECADE DONATION; PAINFUL DEVELOPMENT OF THE BEST IRANIAN OPU

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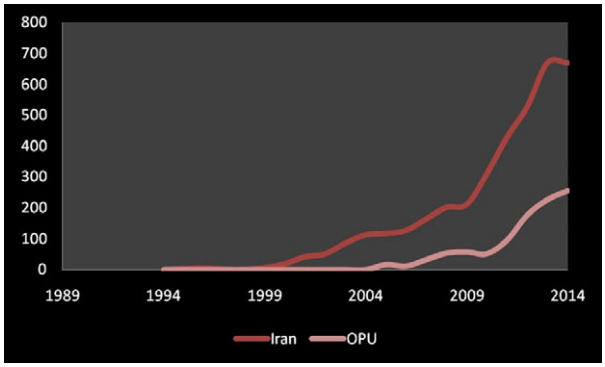
Background: Organ procurement and donation from the brain dead (DBD) in Iran started systematically after the Act of "Organ Transplantation from Deceased Donors" in 2000, 11 years after issuing a decree (*Fatwa*) by Ayatollah Khomeini on its religious permission. Such a long interval indicates many variables influencing DBD in Iran at that period of time and even today. In 2005, Shahid Beheshti Medical University (SBMU), one of three medical universities of Tehran, established its own Organ Procurement Unit (OPU) in Massih Daneshvari hospital.
Method: In this analysis, the statistics of this OPU compared with national and international figures, using the registry of the OPU and Iran Ministry of Health and the International Registry On Organ Donation and Transplant (IRODaT). The progression and regression in OPU activity trend were determined and interpreted.
Results: The main cause of brain death in all DBDs has been head trauma due to car accident (43%). From these cases, 3153 organs have been donated to in-need patients (3.2 organs by average). Since its debut, this OPU has had a continuous growth and became the most leading OPU of Iran. By 2014, the OPU has accomplished 982 successful DBDs, more than 26% of all DBDs done in Iran since 1994 (3772 cases).



In 2009, temporary lack of experienced donation coordinator led to a decline in the procured organs and pushed the OPU heads to hold advanced course on organ donation and procurement with professionals from Spain in 2011 [Transplant Procurement Management]. This measure had good results and raised the number of organ donation. However, in recent years that rising trend has lost its primary momentum.
Conclusion: After a timely emphasis on educating donation coordinators, a solution which has realized most of its potential in expanding donor pool, it is time to think about another ways. Improving case detection ways and macro level cultural and legal measures are to be considered.

BO47 SEUSA PROGRAM: A SUCESFULL MODEL TO DEVELOP A DONATION SYSTEM. THE TRINIDAD AND TOBAGO EXPERIENCE

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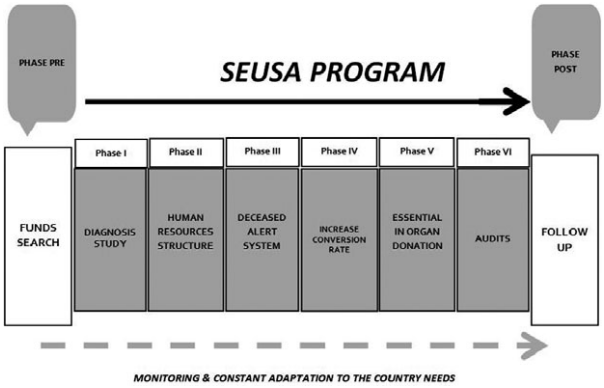
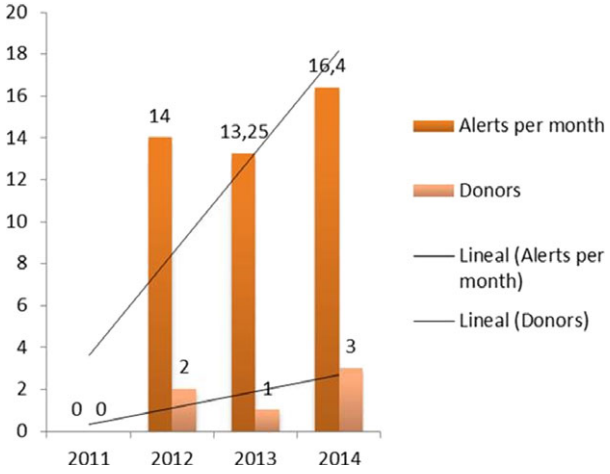
Introduction: In Trinidad and Tobago (T&T) there are more than 500 patients with chronic kidney failure. Kidney transplantation is their unique opportunity to recover their quality of life. World Health Organization (WHO) is advocating for the development of self-sufficiency in Donation and Transplantation (D&T) in all countries, as a practical alternative to combating transplant tourism and commercialism around the world. SEUSA is an international cooperation program to increase the D&T rates. SEUSA methodology is based on three of the successful models in the world (Spanish–European–USA).
Objective: To enhance and consolidate the D&T activities in T&T.
Methods: SEUSA project was implemented in T&T in 2010 with the support of the National Organ Transplant Unit (NOTU) and the Ministry of Health of T&T. The SEUSA program included: a) Diagnosis of the current situation using the ODDS (Organ Donation Diagnostic Surveys); b) Creation of a human resources structure through Transplant Procurement Management (TPM); c) Detection of all brain and cardiac deaths in the hospitals implementing the DAS (Deceased Alert System); e) In-hospital awareness based on the EODS (Essentials in Organ Donation) and f) External hospital audits. Periodic monitoring is performed.



Thanks to SEUSA program 94 health care professionals have been trained in D&T, the Living Kidney Program has been reinforced and the structure of the Deceased Donation network was defined. Since 2010, 328 potential organ donors have been detected, 6 of them had become actual organ donors. 20 patients have received a kidney transplant. In addition, Donation after Cardiac Death (DCD) program is, currently, being organized.



Conclusion: The SEUSA through the previous experience carried out in La Puglia (Italy) and Lebanon has showed, one more time, to be a good option to consolidate the D&T Syste. SEUSA represents a valuable and replicable international collaboration.

BO48 PSYCHOLOGICAL WELL-BEING IN PATIENTS AFTER PREEMPTIVE KIDNEY TRANSPLANTATION

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Background: Preemptive kidney transplantation is associated with improved patient and graft survival as compared to transplantation done in previously dialyzed patients. Preemptively transplanted patients avoid numerous complications related to dialysis. Psychological functioning of those patients is still under investigation. The aim of the following study was to evaluate the acceptance of illness, satisfaction of life and anxiety in patients preemptively transplanted (PET) and transplanted after variable duration of dialysis (PTD).
Material/Methods: The present study compares 22 pairs PET and PTD receiving renal graft from the same donor. Each patient completed a set of psychological questionnaires: Acceptance of Illness Scale (AIS), Satisfaction with Life Scale (SWLS) and State-Trait Anxiety Inventory (STAI). Pairs were examined at the same moment (7 days up to 5 years after transplantation). Results

The PET and PTD groups did not differ significantly in respect of age, gender, underlying renal diseases, incidence of acute rejection, surgical complications and graft function. More PTD patients experienced delayed graft function (Fisher Test, $p < 0.05$). The statistical analysis revealed statistically lower acceptance of illness as well as satisfaction with life in PET recipients (*t*-student test, $p < 0.05$). The groups did not differ significantly in the trait or state of anxiety.
Conclusions: PET who did not experienced any difficulties of dialysis are faced with unexpected discomfort after transplantation resulting in lower life quality as compare to PTD. Particularly in PET effort should focus on providing psychological support during pre transplant counseling and in follow-up after transplantation.

BO49 BALNEOTHERAPY (BT) TOGETHER WITH PHYSICAL REHABILITATION SIGNIFICANTLY INCREASES HEALTH RELATED QUALITY OF LIFE (HRQL) AFTER KIDNEY TRANSPLANTATION

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HRQL is an important outcome following KTx. BT has a potential to become a relevant part of rehabilitation process. Publications concerning this topic are very rare. Aim: To evaluate risks versus benefits of BT after KTx and its impact on HRQL.
Methods: In a retrospective study, we compared 2 groups of Ps. Group A: 53 Ps (34 F) after KTx, median age 51 years (range 24–63), median time after Tx 9 months (3–12). Group B: 60 Ps (41 F) with chronic cystitis, risky for UTI but without immunosuppression and operation, median age 62 years (30–87). All Ps were treated in bath tubes and whirpools for 15 min daily during 20–22 days of their stay in spa, as a part of complex physical therapy. Results

Risks- no significant difference was found in the presence of infectious complications (group A versus B): de novo acute urinary tract infections (UTI) 2 vs. 4 Ps (3.8 vs. 6.7%), de novo acute UTI in women only, 2 vs. 3 Ps (5.9 vs. 7.3%), upper respiratory tract infections 4 vs. 8 Ps (7.5 vs. 13.3%), acute gastroenteritis 2 (3.8%) vs. 0, all p=NS. Infectious complication were a cause of early dismissal in 3 vs. 1 Ps (7.3 vs. 1.7%), p = NS. Not any significant difference was detected in acceleration of hypertension: 4 vs. 1 Ps (7.5 vs. 1.7%), hypotensive episodes: 2 vs. 1 Ps (3.8 vs. 1.7%), or any medical complication during stay at SPA: 18 vs. 16 Ps (34 vs. 27%), all p = NS. Forty eight vs. 59 Ps (91 vs. 98%), p = NS, completed full length of their stay in SPA. Benefits- at the dismissal, all Ps after KTx who completed SPA therapy reported lesser fatigue, bodily pain, improved muscle strenght, raised well-being, vitality and energy.
Conclusion: BT together with physical rehabilitation significantly increased HRQL after KTx. The incidence of complications (either infectious or cardio-vascular) was not significantly different in comparison to other nephrologic/urologic Ps but without immunosuppression. BT as a part of rehabilitation proces should be ofered to Ps after KTx more frequently.

BO50 PSYCHOSOCIAL IMPACT OF DONATION PROCESS: EVALUATION OF LIVING KIDNEY DONOR SATISFACTION

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[1]Fundacio Clinic of Barcelona; [2]Hospital Clínic of Barcelona; [3]LIDOBS Network; [4]Belvitge Hospital; [5]Hospital Universitari Josep Trueta; [6]Hospital Universitari Germans Trias i Pujol; [7]Hospital Universitario 12 Octubre; [8]Complexo Hospitalario Universitario A Coruña; [9]Fundació Puigvert; [10]Hospital Sant Joan de Deú; [11]Universitat de Barcelona

Introduction: Living Donation has a positive impact on Kidney Living donors (KLDs) in terms of their self-estimation and social value. However, an evaluated risk on their physical and psychosocial outcome is presented. Such risk appears to be linearly increased for a longer post donation time. This study was co-founded by European Regional Development Fund (FEDER), 2011–14.
Objective: To analyze the impact of donation process and the level of satisfaction received from the donation process.
Methodology: The population includes the LDs who donated in nine transplant centers all over Spain during the year 2000 till 2010. A retrospective study was conducted to evaluate the satisfaction level KLDs received from the donation process. As assessment tool a new version of the EULID (European Living Donation and Public Health) satisfaction survey was designed using an analogical-visual scale. The questions were addressed to explore: Perception and acceptance of the donation process (information received, decision making and impact of donation on economics, life opportunities, job and donor-recipient relationship).
Results: The centers adapted the methodology to their characteristics and resources. 240 KLDs are included in the study. The most frequent socio-demographic profile was: female, 51 years-old, genetically related with the recipient, full-time employed.The mean time between the donation process and the survey was 5.2 years. The donors perception about the recipient status was good 8.1 (range 0–10). Pearson correlations was calculated to verify that the KLDS opinions not depend of the donor's age nor elapsed time. Pre-donation KLDs experiences more uncertainty than fear ($p < 0.0005$) and more hapiness tan responsibility ($p < 0.0005$).
Conclusion: The LDs satisfaction is key point to ensure the overall quality and security of donation procedures and the key to detect all these potential negative consequences of becoming an Living Organ Donor.

007 DONATION/RETRIEVAL

BO51 DIFFERENCES IN LIVER AND KIDNEY PHYSIOLOGY MEASURED WITH NON INVASIVE (MRI) ASSESSMENT OF TISSUE OXYGENATION AND ORGAN PERFUSION IN BRAIN DEAD RATS

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Background: Brain death (BD) triggers hemodynamic impairment; despite the clinical effort in the last decades no clear improvements in organ quality have been achieved. We studied oxygen consumption and tissue perfusion using a noninvasive strategy based on Magnetic Resonance Imaging.
Methods: BD was induced in eight mechanically ventilated rats by inflation of a Fogarty catheter in the epidural space. As a control group sham operated rats were used. Using an Agilent 9.4 T preclinical MRI system, BOLD sequence and ASL sequences were obtain during experimental time. After 4 h of BD, plasma, kidney and liver tissue were collected. Blood gas analyses and routine biochemistry was performed.
Results: Increases in renal (creatinine, urea) and liver injury markers (AST) in brain death animals were found. Also, plasma values of lactate increased while glucose decreased. Increase in oxygen consumption values in liver tissue but not kidney tissue were found in BD animals. Relative blood flow in the liver did not change during brain death while flow through the kidney decreased during brain death compared to sham operated animals.
Conclusions: Using a non-invasive MR assessment, an increase of oxygen consumption and no changes in perfusion was found in liver tissue during brain death. Contrary, no change in oxygen consumption and a decrease in tissue perfusion was found in kidneys of BD rats compared to sham operated animals. These results suggest that while the liver is metabolically more active during BD, kidneys lack perfusion and therefore may suffer more ischemic injury during BD. Although both organs are facing injurious problems within the same donor, etiology is different. Therefore different strategies to improve quality prior to transplantation are needed.

BO52 HYPERTONIC SALINE SOLUTION REDUCES INFLAMMATION IN RATS SUBMITTED TO BRAIN DEATH: AN INTRAVITAL MICROSCOPIC STUDY

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Heart Institute (Incor), Sao Paulo University Medical School

Background: Brain death (BD) induces hemodynamic instability with microcirculation hypoperfusion leading to increased organ inflammation and dysfunction. This study aimed to investigate the effects of 7.5% hypertonic saline solution on the course of the inflammatory response in rats submitted to BD.
Methods: Male Wistar rats were anesthetized and mechanically ventilated. A balloon catheter was placed into intracranial cavity and quickly inflated to induce BD. Rats were randomly divided into: NS – rats treated with normal saline (0.9% NaCl, 4 ml/Kg) immediately after BD induction; HSS – rats treated with hypertonic saline (7.5% NaCl, 4 ml/kg) immediately after BD; HSS60 – rats treated with hypertonic saline (7.5% NaCl, 4 ml/kg) 60 min after BD. Mesenteric microcirculation was observed by intravital microscopy 3 h after BD induction to evaluate percentage of perfused small vessels (<30 μm), and leukocyte-endothelial interactions. Immunohistochemistry was performed to investigate the endothelial expression of intercellular adhesion molecules.
Results: All groups presented similar hypertensive peak followed by hypotension after BD induction. Proportion of perfused small vessels was increased in both treated groups, HSS (71 ± 9%, p = 0.001) and HSS60 (64 ± 9%, p = 0.004), compared to NS (46 ± 9%). Number of adhered leukocytes was decreased in HSS (2.5 ± 0.5 cells/100 μm, p = 0.02) compared to NS (4.2 ± 0.3). Number of leukocytes migrated to perivascular tissue was reduced in both treated groups, HSS (2.2 ± 0.1 cells/5,000 μm^2, p = 0.006) and HSS60 (2.4 ± 0.1, p = 0.002), compared to NS (3.3 ± 0.1). Both treatments, HSS and HSS60, reduced the expression of ICAM-1 (~30%) and P-selectin (~60%) compared to NS group.
Conclusions: Data presented suggest that treatment of BD rats with hypertonic saline improves mesenteric perfusion and reduces inflammation without hemodynamic changes, even when performed in course of BD progression.
Financial Support: Sao Paulo Research Foundation (FAPESP).

BO53 NEUROGENIC PULMONARY EDEMA AND RIGHT VENTRICULAR DYSFUNCTION IN AN ANIMAL MODEL OF BRAIN DEATH

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[1]CHU Dinant-Godinne UCL; [2]Physiopathology Laboratory ULB; [3]Anatomopathology Laboratory - ULB - Erasmus Hospital

Introduction: Brain death (BD) triggers sympathetic storm with a torrent of circulatory catecholamines. Neurogenic pulmonary edema (NPE) and ventricular dysfunction can be achieved in return. Inflammation may be implicated in the pathogenesis of the condition but its precise role remains uncertain. We developed a model of brain death in pig to study the development of NPE and right ventricular (RV) dysfunction.
Methods & Results: Sixteen pigs were randomized to placebo (n = 9) or corticosteroids (n = 7) 1.5 mg/kg before BD induced by slow intracranial blood infusion. Four hours after BD, the animals underwent a hemodynamic evaluation followed by lung and RV tissue sampling for rtq-PCR for the inflammatory modulator HO-1 and the pro-inflammatory ratio IL-6 / IL10, and lung histopathologic injury score. A control group (n = 9) was studied. After 4 h, BD increased cardiac frequency, pulmonary pressure, pulmonary vascular resistance, pulmonary arterial impedance at 0 Hz, and capillary pressure.Right ventricular end-systolic elastance (Ees) increased but not in proportion to pulmonary arterial elastance (Ea) so that Ees/Ea ratio decreased.Systemic arterial pressure was decreased while cardiac output, occluded pulmonary arterial pressure, right auricular pressure and characteristic impedance did not change. The ratio of partial pressure arterial oxygen and fraction of inspired oxygen collapsed. BD was associated with an increase in IL-6/IL-10 and with a decrease in HO-1 gene expression in lung and RV tissue.BD increased the lung injury score.
Conclusions: BD causes lung injury pulmonary and RV dysfunction associated with up-regulation of IL-6/IL-10 and down-regulation HO-1.

BO54 THE DURATION OF BRAIN DEATH INDUCTION IN RATS LEADS TO DIFFERENCES IN INFLAMMATORY AND APOPTOTIC RESPONSES IN ABDOMINAL ORGANS

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Background: Donor brain death (BD) is an independent risk factor for primary and delayed renal graft function. Furthermore, the speed of onset of brain death, traumatic (fast) or hemorrhagic (slow), influences graft function after transplantation. No explanation has been reported so far to explain the differential effect of cause of donor BD on renal graft function. This study was conducted to elucidate potential underlying processes initiated by either sudden or gradual brain injury leading to BD.
Methods: Slow and Fast BD induction was performed in 64 mechanically ventilated male Fisher rats by inflating a 4.0F Fogarty catheter in the epidural space. Rats were observed for 0.5 h, 1 h, 2 h, or 4 h following BD induction. Slow induction was achieved by inflating the balloon-catheter at a speed of 0.015 ml/min until confirmation of BD after approximately 30 min. Fast induction was achieved by inflating the balloon at 0.45 ml/min for 1 min. After the observation period, plasma, liver and kidney tissue were collected. RT-qPCR and routine biochemistry were performed.
Results: Slow induction led to a consistent drop in BP below 60 mmHg during induction whereas fast induction led to a rise in BP above 150 mmHg. Fast induced BD animals required more inotropic support during the first hour of BD. Plasma creatinine values were significantly higher in slow inducted animals at 2 h and 4 h of BD. Urea and liver injury markers increased over time in both models. Interleukin 6 (IL-6) plasma levels were higher in slow induction animals after 1 h of BD in both models there was an increase in IL-6 plasma levels and inflammatory related genes over time.
Conclusion: Slow induction brain death leads to increased renal inflammation and creatinine levels. Hemodynamic impairment in the slow induction model may explain the difference between both BD models. However, both models lead to increased expression of inflammatory markers and poor liver and kidney quality markers.

BO55 SEX DIFFERENCES ON DONOR LEUKOCYTE MOBILIZATION AND ORGAN INFLAMMATION AFTER BRAIN DEATH

Ana Cristina Breithaupt-Faloppa, Ferreira Sueli Gomes, Kudo Guilherme Konishi, Simão Raif Restivo, Roberto Armstrong Jr, Paulina Sannomiya, Luiz Felipe Moreira

Heart Institute (Incor – HC) Sao Paulo University Medical School

Background: The importance of sex in organ transplantation is evidenced by reports showing reduced survival of male recipients with female grafts. Understanding the impact of female sex hormones on the donor state and on the inflammatory process triggered by brain death (BD) is particularly important. In this study, we investigated the sex differences in the leukocyte mobilization from bone marrow to blood and tissues.
Methods: Wistar rats were divided into 3 groups: male, female (from high estradiol secretion to heat period) and ovariectomized female (OVx). Ovariectomy was carried out 10 days before BD. BD was induced using intracranial balloon rapid inflation. Bone marrow and white blood cell counts were analyzed after 6 h of BD. Serum concentrations of estradiol, progesterone and CINC-1 were quantified by ELISA. Heart, lung, liver, kidney and intestine samples were collected, sectioned and stained for histological analysis. Leukocyte infiltration, edema and hemorrhage were investigated.
Results: Female rats presented significant reduction of the bone marrow cell number in comparison to male rats ($F = 58.4 \pm 10.99$, $M = 115.6 \pm 20.2$; $p = 0.026$). The male group, however, presented leukopenia (Male initial: 13475 ± 920; 6 h: 9588 ± 1174, $p = 0.04$) while female and OVx maintained the circulating leukocyte numbers. CINC-1 concentration was significantly higher in the female group compared to other groups ($F = 675 \pm 75.2$, $OVx = 320.7 \pm 61.92$, $M = 269.7 \pm 66.69$ pg/ml; $p = 0.021$). Regarding the histological analysis, female presented increased leukocyte infiltration in lung, heart and intestine compared to male. Hemorrhage in the lungs was higher in the OVx group compared to the other groups and the edema was significant in the female in comparison to male.
Conclusion: The organ inflammation in brain dead female rats can be a result of the association of female sex hormones, higher CINC-1 levels and circulating leukocyte numbers.
Financial Support: São Paulo Research Foundation (FAPESP 2013/20282-0).

BO56 PULMONARY MICROCIRCULATION COMPROMISE AFTER BRAIN-DEAD INDUCTION IN RATS: AN INTRAVITAL MICROSCOPY STUDY

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Background: Brain death triggers important hemodynamic and inflammatory alterations, and it is associated with organ dysfunction, compromising the viability of organs suitable for transplantation. This study is the first to investigate pulmonary microcirculatory alterations in brain-dead rats.
Methods: Male Wistar rats (300 ± 30 g) were anaesthetized and mechanically ventilated. Brain death was induced by rapid inflation of a catheter Fogarty®3F and confirmed by maximal pupil dilatation, apnea, absence of reflex, and drop of mean arterial pressure ($n = 5$). Rats trepanned only were used as control group ($n = 5$). Expiratory O2 and CO2 were monitored and after 3 h, a thoracotomy was performed, and a window was created to observe the lung surface. Using an epi-fluorescence intravital microscopy, the pulmonary microcirculation was observed and the number of vessels with blood flow was determined in an area of 200 000 μm^2.
Results: Three hours after the surgical procedures, pulmonary perfusion was 73%in the control group. On the other hand, brain-dead animals showed an important decrease in organ perfusion to 28% at the same period ($p = 0.036$). This important organ hypoperfusion was associated with a reduction in the expiratory CO2, from 2.9% to 1.47% ($p < 0.001$), situation that did not occur in control group animals ($p = 0.002$).
Conclusions: The data presented in this study show that brain death itself triggered an important pulmonary hypoperfusion, that was associated with organ dysfunction 3 h after its induction.

BO57 TARGETING METABOLIC PATHWAYS IN BRAIN DEAD DONORS TO IMPROVE OUTCOMES OF KIDNEY TRANSPLANTATION

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Introduction: Donation after brain death (DBD) organ donors remain an importance source of kidneys for transplantation. However, during the brain death process kidneys are injured making them more susceptible to warm and cold ischemia. Understanding how this injury can be abrogated is of importance, especially from older and more marginal donors. We describe novel targets for therapeutic intervention in the brain dead organ donor.
Methods: Using a rodent model of brain death we evaluated cellular and molecular pathways that were altered following brain death in comparison to controls, using novel proteomic (GC-MS) and metabolomic technologies (1H-NMR).

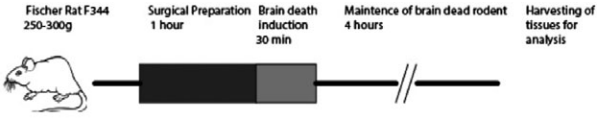

Fig 1. Schematic of the brain death model. Mean arterial pressures maintained between 80-120mmHg following brain death.

We validated our findings and characterised the interaction of disturbances in metabolic pathways on mitochondria, oxidative stress and hypoxia inducible factors (HIF).
Results: Our results demonstrated higher amounts of anaerobic metabolic intermediaries, including lactate ($p = 0.04$) and higher dependency of the brain dead donor kidneys on non-oxidative phosphorylation pathways, such as fatty acid metabolism (Fig 2). We demonstrated a build up of TCA cycle intermediaries such as succinate ($p = 0.04$), a correlation between metabolic stress and alteration of mitochondrial respiration at complex IV ($p = 0.02$) and production of reactive oxygen species ($p = 0.01$). A correlation between the degree of haemodynamic instability in the donor and HIF1α was found (Fig 2. $p = 0.01$).

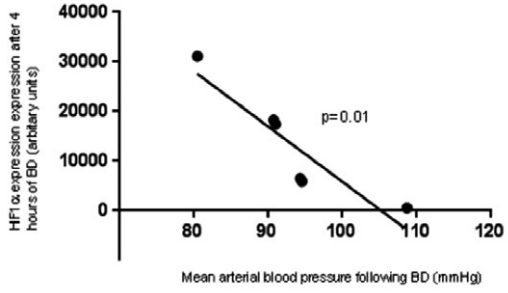

Fig 2. Spearman correlation and linear regression of correlation between HIF1α expression and post brain death mean arterial pressure (MAP)

Discussion: Brain death results in alteration of metabolic pathways in the kidney leading to altered mitochondrial respiration and oxidative stress. Metabolic conditioning is a possible intervention that can be instigated during management of the brain dead organ donor and may improve the outcomes of transplantation.

BO58 LYMPHOCYTE SUBSETS, EXPRESSION OF ADHESION MOLECULES AND APOPTOSIS IN BONE MARROW CELLS OF BRAIN-DEAD RATS

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Background: Brain death (BD) induces a progressive leucopenia and reduction in the number of bone marrow cells. In this study, we evaluated bone marrow lymphocyte subsets, granulocyte adhesion molecules and bone marrow cell death in rats submitted to BD compared with BD-associated trauma.
Methods: Male Wistar rats (250–350 g) were anesthetized and mechanically ventilated. After trepanation, a balloon catheter was placed into intracranial cavity and quickly inflated to induce BD ($n = 5$). Sham operated rats (SH, $n = 5$) were trepanned only. After 6 h, bone marrow cells were harvested by flushing the femoral cavity with Iscove's medium. Bone marrow cells (1×10^6) were incubated with mAbs against CD3, CD4, CD5 and CD8 to characterize lymphocyte subsets; mAbs against CD11a, CD11b/c and CD62L to investigate expression of beta2-integrins and L-selectin on granulocytes. Apoptosis and necrosis were evaluated using annexin V-FITC and propidium iodide (PI) protocol. Cells were acquired using FACSCanto II and analyzed by FlowJo.

Results: Bone marrow lymphocyte subsets were similar in both BD and SH rats (CD3, p = 0.1; CD4, p = 0.4; CD3/CD4, p = 0.4; CD5, p = 0.4; CD3/CD5, p = 0.2; CD8, p = 0.8). The expression of beta2-integrins and L-selectin on granulocytes did not differ between BD and SH groups (CD11a, p = 0.9; CD11b/c, p = 0.7; CD62L, p = 0.1). Percentage of apoptosis and necrosis of bone marrow cells did not differ between groups (Annexin V, p = 0.73; PI, p = 0.21; Annexin V/PI, p = 0.29).
Conclusions: Data presented suggest that the down-regulation of the bone marrow triggered by BD is not related to differences in lymphocyte subsets, expression of granulocyte adhesion molecules, or bone marrow apoptosis and necrosis.
Financial Support: Grant 2011/22803-2, São Paulo Research Foundation (FAPESP).

BO59 BARIATRIC OPERATIONS AT A SERVICE OF THE TRANSPLANT SURGERY

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Introduction: Bariatric operations in the peri-transplant setting could be done at different stages – organ donor, prospective organ recipient, transplanted patients, all in order to extend graft availability and graft survival and reduce morbidity. Different bariatric operations can be used in different settings. We examined the effectiveness and safety of bariatric operations in recipients, donors, and transplanted patients in liver, kidney and heart transplantation.
Methods: We collected all bariatric procedures performed as a preparatory step in these three groups between April 2011 and March 2015 in our center. The data included demographics and graft function, weight, BMI, EWL, and morbidity. Mean follow-up duration was 18 months (2-47).
Results: 40 patients underwent bariatric operations (13 - gastric bypass, 28 sleeve gastrectomy, 1- duodenal switch, 2 underwent two procedures). 29 patients involved in the Kidney transplant (five donors, five future recipients(on dialysis), 19 transplanted patients); 8 in the liver, (four cirrhotics, three after OLT, and one – simultaneous liver transplantation with sleeve gastrectomy); three in heart (two listed candidates, one of them on LVAD, one heart transplanted patient).Among all the transplanted (group 3, all organs, 24 pateints) patients mean preoperative weight and BMI were 118 kg(104–152 kg) and 42 kg/m^2 (38–50 kg/m^2), respectively. Mean postoperative weight and BMI were 84(60–145) and 33(23–48), respectively. The EWL was 54(9–81%). There was one short term and one long term weight loss failures. There were four major complications (17%) - intraabdominal bleeding, one anastomotic leak (OLT patient), one stricture and transient CRF. No rejection or graft dysfunctions were encountered. Two prospective heart recipients (group 2) were delisted due to mprovement. Three - donated kidneys.
Conclusions: In this series, bariatric operations appear to be effective and safe in peri-trasplant setting.

BO60 SIMULTANEOUS LIVING DONOR KIDNEY AND PARATHYROID ALLOTRANSPLANTATION

Sandra Garcia Aroz, Raquel Garcia Roca, Ivo Tzvetanov, Enrico Benedetti
UIC

Introduction: Congenital hypoparathyroidysm results in severe hypocalcemia frequently complicated by multiorgan calcinosis and possible renal failure. Oral supplementation of calcium and vitamin D may be insufficient to prevent complications. Parathyroid transplant should be considered as a physiological cure, especially in the setting of renal transplantation, which justify the need for immunosuppression.
Case: A 23-year-old female with end-stage renal disease secondary to a rare form of congenital hypoparathyroidism was referred for kidney transplantation. She had experienced serious complications including: severe tetany, seizures, metabolic acidosis, calcium induced pancreatitis and renal stones. She was highly dependent on calcitriol, calcium (6 gm/day) and magnesium supplements with undetectable serum intact parathormone (iPTH). Her healthy sister volunteered for kidney and single parathyroid gland donation, both procured robotically. The procurement of the parathyroid gland was completed through a cosmetic trans-axillary approach. The donor recovered well without complications. Parathyroid gland was confirmed by pathology and implanted in the rectus muscle during the exposure to kidney transplantation. She received Basiliximab induction therapy, 5 day prednisone taper and was maintained on Tacrolimus and mycophenolic acid. The iPTH was first detected and then noted to steadily increase (Table 1). After 7 months she remains asymptomatic, with excellent renal function (creatinine 1.3 mg/dl), with normal calcium level on only 2gm of oral calcium; the serum iPTH is currently 26 pg/ml (normal 14–72 pg/ml).
Conclusion: We report the first robotic simultaneous living donor kidney and parathyroid transplant from a healthy donor. Single gland robotic parathyroidectomy in addition to robotic nephrectomy was well tolerated by the donor. The procedure is well justified in patients with refractory hypocalcaemia requiring kidney transplant related long term immunosuppression.

001 ALLOCATION

BO61*

RANK OF SURVIVAL BENEFIT, AS A PROPOSED PRIORITY SYSTEM, IN LIVER TRANSPLANT WAITING LIST: EVIDENCES FROM AN ITALIAN MULTICENTRE COHORT STUDY

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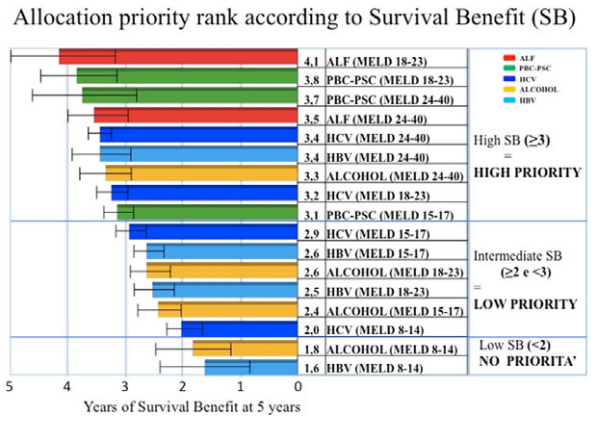
Post transplant Survival benefit (SB) has been recently proposed in US for measuring the outcome of pts listed for liver transplantation (LT). However, its translation into allocation rules is still lacking. Moreover, a large European multicentre study on SB has not been performed so far.

A database of 3010 consecutive cases listed for LT in 4 centres (2002–2012) was built. 312 pts (10%) were excluded for age limits (1%), rare indications (1%), inconsistencies (8%). The remaining 2698 pts constituted the study population. 2110 pts (78%) were transplanted (TX).

Preliminary statistical analysis identified age, MELD, primary indication, Transplant Centre code as significant outcome-predictive factors. Primary indication strata were cirrhosis due to HCV, HBV, alcohol, PBC-PSC, and Acute Liver Failure (ALF). Since HCC was present as a co-indication in 37% of the cases, and missing data on HCC stage were up to 27%, HCC could not be utilized in the stratification model. To avoid biases, the propensity score match (PSM) test was performed utilizing recipient age, year of listing, transplant centre code as covariates. 4 MELD classes were identified with quartile approach and primary-indication stratification. The final study population obtained after PSM consisted of 1183 pts (44% of the initial study population). 591 pts were transplanted (treated arm) and 592 remained on the waiting list (control arm). For each MELD-primary indication subclass, the SB was calculated as the difference between the area under the curve of the TX group and that of the waiting list group. The SB was calculated at 5 years. The highest SB was obtained in MELD 18-23 ALF sub-class, the lowest in MELD 8-14 HBV sub-class. Being aware that SB is a continuous variable, classes were arbitrarily divided in 3 priority levels for practical reasons.



The SB methodology allows an effective stratification of the priority rank. An external validation is mandatory before the translation into allocation rules.

BO62

SURVIVAL OUTCOMES FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION USING THE BALANCE OF RISK SCORE (BAR) IN A TRANSPLANT CENTER IN CHILE

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Background: Nowadays, most of liver transplant candidates are prioritized by their highest model for end-stage liver disease (MELD) score, due to its accuracy to predict mortality on the waiting list. However, several transplant centers are reporting that the "sickest first" policy would decrease long-term survival after orthotopic liver transplantation (OLT). In this context, a recent multicentric study validated a score that combines 6 key independent donor and recipient factors, in order to improve graft allocation in liver transplantation.

Objective: To evaluate the impact of recipient characteristics assessed by MELD score, donor and graft factors by DRI (Donor Risk Index) score and both by BAR (Balance of Risk Score) on long-term survival after OLT in a Transplant Center in Chile.

Patients and Methods: Retrospective study, using clinical data from OLT performed between January 2003 and August 2013 in our Institution. MELD, DRI and BAR scores at transplantation were calculated for each procedure. Survival analysis for each score was performed using Kaplan Meier curves and Log rank test. Results were considered significant at a p-value of <0.05.

Results: During the study period a total of 144 transplant procedures were performed in 138 patients, 63% male with a median age of 58 year old (16–71). Recipients with a MELD score at transplantation ≤ 15 and >15 had a 5 year-survival rate of 71% and 70%, respectively ($p = 0.39$). Graft/donor DRI score ≤ 1.4 showed a better 5 year-survival after transplant (76%) compared to a >1.4 score (64%), although it was not statistically significant ($p = 0.24$). Unlike MELD or DRI, BAR score predicted accurately 5-year survival following OLT ($\leq 15 = 76\%$ vs. $>15 = 40\%$; $p < 0.001$)

Conclusions: The BAR score could help determine in real time the fitter candidates for OLT in our Center and together with MELD, better quantify survival benefit for individual transplant procedures.

BO64

NEW ORGAN ALLOCATION SCORE PREDICTING BOTH PRE AND POST-TRANSPLANT SURVIVAL IN THE ROMANIAN NATIONAL TRANSPLANT PROGRAM

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Fundeni Clinical Institute

Background: An ideal liver allocation system should reduce waitlist mortality and also improve posttransplant survival. Considering survival benefit, MELD score is an inaccurate predictor of posttransplant survival. Aim: To identify a new scoring system that predicts recipient survival at 3 months following liver transplantation (LT) in the Romanian LT program, as well as its use as a graft allocation system.

Methods: We included into analysis 242 adult patients (183 patients within the training set and 59 in the validation cohort) with liver cirrhosis consecutively transplanted between January 2012 – June 2014. Another 175 patients represented the validation set for predicting waitlist mortality. We formulated a score to predict 3 months survival outcomes following LT (RoSOFT) that includes both donor and recipient factors to evaluate transplants at the time of LT.

Results: Posttransplant overall survival was 84.2% at 3 months. Recipients with HCC outside Milan criteria had a significantly lower MELD score at LT compared to patients with HCC inside Milan ($p = 0.008$, 14.6 ± 3.9 vs. 17.1 ± 5.1) and received a higher proportion of marginal organs ($p = 0.005$, 65.4% vs. 27.9%), but survival after LT did not differ ($p = 0.47$). Independent risk factors for survival following LT were: recipient age >53 years ($p = 0.01$), serum albumin <2.7 g/dl ($p = 0.02$), diabetes mellitus ($p = 0.14$), hyponatremia <130 mmol/l, presence of non-malignant portal vein thrombosis ($p = 0.01$), retransplantation ($p = 0.0005$) and donor resuscitation following cardiac arrest ($p = 0.03$). AUROC of RoSOFT score is 0.86 in both training and validation set. Diagnostic accuracy of RoSOFT for predicting 3 months mortality is 89.6%. AUROC for ROSOFT score is 0.95 in predicting 6 months mortality on the waiting list.

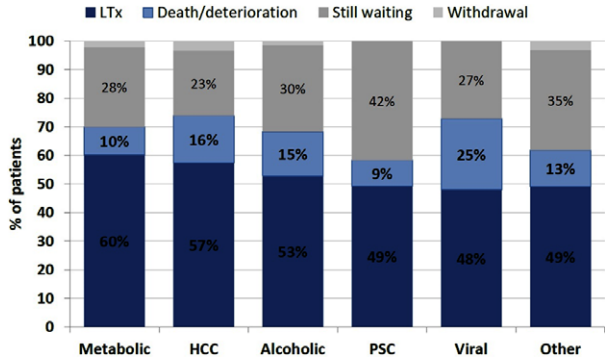
Conclusions: Combined recipient and donor risk factors can accurately predict 3-months survival following LT in our National LT Program and can improve donor-recipient matching as well as organ allocation.

BO65 WHAT IS MY CHANCE TO GET A DONOR LIVER IN TIME?

Madelon Tieleman[1], Bart Van Hoek[2], Aad Van Den Berg[3], Wojciech Polak[1], Jan Ringers[2], Robert Porte[3], Rob De Man[1], Cynthia Konijn[4], Bettina Hansen[1], Herold Metselaar[1]

[1]Erasmus University Medical Centre; [2]Leiden University Medical Centre; [3]University Medical Centre Groningen; [4]Dutch Transplantation Foundation

Introduction: Waiting for a donor liver is a time of insecurity for patients, with the most asked question "Will the transplant be in time". The MELD score of the patient and the availability of donor livers primarily determine this. We wondered whether patients with different liver diseases have the same chance for liver transplantation (LTx) in the first year of listing. Therefore, we analysed the outcomes of patients placed on the waiting list (WL) in the Netherlands.
Methods: Patients listed for first LTx on the WL between December 16th, 2006 and December 31th, 2013 were included. Patients with acute liver failure or combined organ transplantation were excluded. Outcome measures were LTx, death or removal due to deterioration, withdrawal due to other reasons and still waiting. Survival analysis was computed with competing risk analyses and adjusted for sex and blood type.
Results: 852 patients (median age 54 years; M/F 579/273) were listed with the following indications: HCC in 237 patients, PSC in 146 patients, alcoholic liver disease in 142 patients, metabolic liver disease in 93 patients, viral hepatitis in 77 patients and other indications in 157 patients. The probabilities of outcomes at 1 year from listing are shown in figure 1. Patients with metabolic liver disease had the highest chance of being transplanted (60%; overall $p = 0.022$). Patients with viral hepatitis had the highest risk of death/deterioration (25%; $p \leq 0.020$ to HCC, PSC, metabolic, other). PSC patients remained significant longer on the WL (42%; $p \leq 0.002$ to alcoholic, HCC, viral, metabolic). There was no significant difference in MELD score at listing between indications for patients who died/deteriorated, except for patients with HCC.
Conclusion: These data show that patients with metabolic liver disease have the highest chance of receiving a liver transplant. Patients with viral hepatitis have the highest risk of death or deterioration and PSC patients remained longer on the waiting list.



BO66 LIVER TRANSPLANT IN HIGH RISK CANDIDATES – FUTILE OR UTILITY DRIVEN?

Andrea Schlegel[1], Michael Linecker[1], Andrea Wirsching[1], Michelle L. Deoliveira[1], Beat Müllhaupt[2], Pierre-Alain Clavien[1], Philipp Dutkowski[1]

[1]Department of Visceral and Transplantation Surgery, University Hospital Zürich; [2]Department of Gastroenterology and Hepatology, University Hospital Zürich

Objectives: Allocation of liver graft triggers emotional debate, as those patients not receiving an organ are prone to death. Most countries have switched to allocation of a specific graft to a patient by severity rather than to a center with the freedom to use the graft to their "best" recipients. Liver allocation by MELD, however, directs grafts to sicker patients, and as a consequence many candidates present nowadays with multi-organ failure at the time of liver transplantation (LT).
Methods: We analyzed a high MELD cohort (lab MELD≥30, $n = 100$, median lab MELD of 34 (IQR: 31–37) of LT recipients transplanted in our center over the last 10 years. Endpoints of our study were morbidity, cost, post-transplant kidney and liver function. Median follow up was 3.5 years.
Results: Median ICU and hospital stays were 8 and 26 days, respectively, after LT, with a high morbidity (median comprehensive complication index 52.6 points (max point: 100) and high cost (median 146.300€)). Kidney function was impaired already at transplant in 76%, and 45% of patients needed hemofiltration before and during transplant (median dialysis time before LT: 13 days). Consistently, 65% of cases required postoperatively hemofiltration (median 16 days). Kidney function, however, recovered completely within 3 months in 95% of cases. One year after transplant, only 5% of patients remained on dialysis, and two patients eventually received a kidney transplant. Five-year outcome of kidney function was excellent (GFR>60 ml/min, median creatinine of 101 μmol/l) and patient survival rates after 5 years were not different, when compared to ELTR cohorts (71 vs. 73%).
Conclusions: While high MELD recipients demonstrate higher morbidity and cost, outcome appears comparable in the long-term, and there is no need for later kidney replacement. Based on this observation, high MELD liver transplants remain justified.

BO67 THE UK ALLOCATION SCHEME FOR KIDNEYS DONATED AFTER CIRCULATORY DEATH

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Background: Until 2014 kidneys from Donors after Circulatory Death (DCD) in the UK were allocated according to local arrangements and acceptance criteria varied between centres resulting in under-utilisation. Transplants using DCD kidneys now account for 40% of all deceased donor kidney transplants and evidence from a Lancet paper by Summers et al(1) found that DCD kidneys were an excellent option for transplantation despite a higher incidence of delayed graft function.
Methods: Following extensive statistical analysis and evidence-based discussion, a new DCD Kidney allocation scheme was implemented on 3 September 2014 to allocate DCD kidneys within 4 pre-defined regions of the UK using the 2006 UK DBD Kidney Allocation Scheme protocols(2). It will be phased in over a number of years to avoid sudden activity changes within transplant centres. The scheme allocates one kidney from all DCD donors primarily to the local centre, with the second kidney only being offered to other centres on a regional basis, initially only for donors aged 5–49 years.
Results: Analysis of the allocation scheme 6 months after its introduction showed an increase in both DCD kidney donor and transplant activity. Of kidneys allocated through the scheme (donors aged 5–49): 51% were shared regionally compared with 32% in the year prior to the scheme; better matching has been achieved with 7% of kidneys transplanted with 1 DR and 2B or 2DR HLA mismatches compared with 17% in the previous year; and cold ischaemia time (CIT) has fallen from 13.5 to 12 h.
Conclusions: The scheme was designed to improve equity of access, optimise utilisation through formalised offering and maintain (or reduce) overall CIT. Initial analysis reveals that the scheme is meeting these objectives.

1. Lancet 2010; 376: 1303–1311.
2. Transplantation 2010; 89: 387–394.

BO68 MORTALITY OF PATIENTS SUSPENDED FROM THE KIDNEY TRANSPLANT WAITING LIST IN THE UK

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Aim: Mortality of patients active on the Kidney Transplant Waiting List (KTWL) considered to be low; this may underestimate true mortality of kidney transplant candidates as some may die after being suspended. We analysed outcome and survival all Suspended Patients (SPt) from KTWL
Method: Using data from UK Transplant Registry (1/1/2000-31/12/2008), we generated 3 Cohorts (Cht)

Cht1: all SPt for a period of >1 month irrespective of activation date.

Cht2: all patients first registered in the study period with suspension of >1 month. Patients censored at transplant or if alive and removed from KTWL. We analysed mortality and suspension rate and their risk factors after Deceased Donor Renal Transplant (DDRT).

Cht3: all patients within Cht2 who survived >1 year from registration. Follow up ≥5 years. Data compared using Kaplan-Meyer for survivals and Cox Model for risk of suspension and death.
Results: Cht1:7516 SPt total, 2566(34%) died, 1125(15%) removed from KTWL. Age most important risk factor.

Cht2:14283 activated patients total, 10493(74%) transplanted, 1192(8.3%) removed from KTWL. Total SPt 6164(43%); 1494(24.2%) SPt died. Total Not

Suspended Patients (NSPt) 8119 (56.8%); 641(8%) NSPt died. Overall 2135 patients died in the study period (15%).

Rate SPt increased with years on KTWL

Survival time	1 year	3 years	5 years
N. Surviving	10098	5313	2253
N. Suspended (%)	2498 (24)	2852 (53)	1162 (74)

Age and primary disease important risk factors for suspension.

5 year survival after DDRT showed no difference between SPt and NSPt; log-rank $p = 0.3$.

Cht3: 5 year survival SPt in 1st year inferior to NSPt; log-rank $p < 0.0001$.

BO69 INTEGRATED CLINICAL-HISTOLOGICAL (ICH) SCORE SYSTEM FOR THE EVALUATION OF "MARGINAL" DONORS IN KIDNEY TRANSPLANTATION

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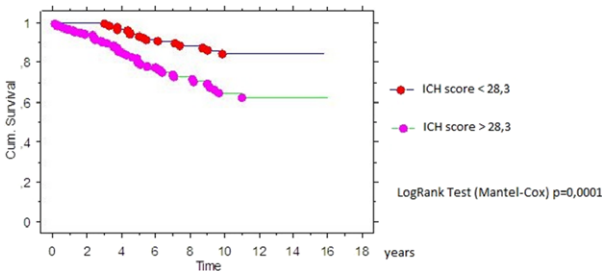
Introduction: The organ shortage has led to increase the procurement of kidney from "marginal" donors and to improve the strategies to better evaluate the quality of these organs. The aim of this study was to identify an integrated clinical-histological (ICH) score that might improve the allocation of organs derived from marginal donors.

Patients and Methods: In a retrospective study, we analyze 326 recipients of single kidney transplantation from deceased donors, randomized in a Training Set ($n = 120$) and a Test Set ($n = 206$). We correlated clinical and histological variables with the glomerular filtration rate (GFR) at 12 months by linear regression in the Training Set; variables with $p < 0.05$ were included in a multivariate analysis.

Results: The variables that statistically correlated with the 1-year renal function were donor age and total histological score ($p < 0.05$). Therefore, we defined an ICH score using the coefficients obtained by regression model: Score = (donor age x 0.5) + (total histological score x 3.4). Appling this ICH score system to the Test Set, the comparison of ROC curves between ICH score and the histological score showed a significant difference and ICH score was the most accurate (comparison between AUC = 0.099, $p = 0.008$). The ROC curve of ICH score has also defined a cut-off of 28.3 (sensitivity 86,2%, specificity 60%). Kaplan–Meier curves showed that patients with ICH score <28.3 have a better 10-years graft survival (85% vs. 65%, LogRankTest $p = 0.0001$).



Conclusions: Our analysis show that the combination of clinical and histological data in an ICH score might significant improve the ability to allocate kidney from marginal donors.

BO70 NEOPLASTIC RISK DONORS: ORGAN PROCUREMENT AND TRANSPLANT ACTIVITY IN THE EMILIA-ROMAGNA REGION

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Introduction: The "neoplastic risk donor" protocol was implemented in Italy in 2003. It refers to transplants (tx) from organ donors having either present or past neoplasia. Aim of this study is to review neoplastic risk donor organ procurement and related tx carried out from 2006 to 2014 as well as recipient survival.

Materials and Methods: All neoplastic risk utilized donors and all organs with related tx from the 1st of January 2006 to the 31st of December 2014 have been reviewed. Recipient survival of tx carried out between 2006 and 2013 (1 year) and between 2006 and 2009 (1 and 5 years) has been analyzed.

Results: 31 neoplastic risk utilized organ donors with 36 donated organs in all (29 livers, 4 kidneys, 2 lungs and 1 heart) were reported between the 1st of January 2006 and the 31st of December 2014. The most frequently affected organs were: Prostate (25.8%), Kidney (25.8%), Central Nervous System (9.7%), Bladder (6.5%), Blood (6.5%), Thyroid (6.5%) and Uterus (6.5%). In this period 35 recipients were transplanted with the 36 organs. 15 tx were carried out between 2006 and 2009 (all of them were liver tx); 12 out of 15 (80%) were living after 1 year, 7 out of 15 (46.7%) were living after 5 years; no deceased recipient died for neoplasia transmission. 33 tx were carried out between 2006 and 2013 (27 liver tx, 4 kidney tx, 1 double lung tx and 1 heart tx); 28 out of 33 (84.8%) were living after 1 year; even in this case no deceased recipient died due to neoplasia transmission.

Conclusions: Over the last years we faced an increasing average of utilized donors in the Emilia-Romagna region (63 years old in 2014); thus the probability of utilizing neoplastic risk donors also increases and will increase in the next years. Low risk of neoplasia transmission between donor and recipient seems to emerge by this study provided that the dedicated protocol are rigorously respected.

015 INFECTIONS

BO71 EFFICACY AND SAFETY OF LOW DOSE VERSUS FULL DOSE VALGANCICLOVIR FOR PREVENTION OF CYTOMEGALOVIRUS DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

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Prophylaxis for cytomegalovirus (CMV) infection is highly recommended for kidney transplant recipients. Using 900 mg daily is the standard advice for such patients while using 450 mg daily was investigated and found equally effective with fewer side effects in some studies.Our aim was to assess the efficacy and safety of 450 mg valgancyclovir prophylaxis compared with 900 mg for kidney transplants.

Methods: We prospectively randomized recent kidney transplants (1:1) to receive 450 mg valgancyclovir prophylaxis (group1) or 900 mg daily (group2) for the first 6 months post-kidney transplant. Patients were studied for incidence of CMV disease, leucopenia attacks, rejection episodes and graft outcome over 1 year duration.

Results: Demographic features of group1 ($n = 100$) and group2 ($n = 101$) were identical. About 50% recipients received thymoglobuline induction without difference between the groups. More patients have received tacrolimus in group1, while in group 2 more patients were maintained on cyclosporine ($p = 0.001$). There were more leucopnia attacks in group 2 ($p = 0.04$) requiring higher doses of granulocyte stimulating factor ($p = 0.03$). Gruop 2 patients received lower doses of mycophenolate mofitel ($p = 0.04$) and reduced doses of valgacyclovir ($p = 0.07$). Group 2 patients have developed more rejection episodes ($p = 0.01$). In group 2; there were more CMV infections requiring full treatment ($p = 0.052$) and more BK virus nephropthy ($p = 0.03$). Graft and patient outcomes were satisfactory in both groups. Mean estimated glomerular filtration rates were above 60 ml/min at baseline, at 6 months and at 12 months post-transplant for both groups.

Conclusion: Using low dose valgancyclovir for post-renal transplant CMV prophylaxis is more effective and safe than using full dose. On low dose prophylaxis, patients had less leucopenia attacks and consequently less manipulation of chemoprophylactic and immunosuppressive drugs which led to fewer rejection episodes and less CMV infections over 1 year of follow up.

BO72 FAVORABLE LONG-TERM OUTCOME OF LATE-ONSET CMV DISEASE IN D+R− KIDNEY TRANSPLANT RECIPIENTS TREATED WITH UNIVERSAL PROPHYLAXIS

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Both universal prophylaxis and preemptive strategies are viable approaches for the prevention of cytomegalovirus (CMV) disease after organ transplantation. Universal prophylaxis is used in most of the centers but leads to higher incidence of late-onset CMV disease (l-od), which has been associated with poor patient and graft survival in kidney transplant recipients (KTR). This retrospective study reappraised the impact of l-od in KTR with the highest risk for CMV infection, i.e. CMV seronegative recipients transplanted with a seropositive donor (D+R−). CMV DNAemia was measured using a whole blood CMV quantitative nucleic acid amplification assay. Early-onset disease (e-od) was defined as occurring before 3 months and l-od after 3 months post-transplantation. Recurrence was defined as a new CMV DNAemia with clinical symptoms, after a successfully treated disease. According to the period, either universal prophylaxis for 3–6 months or preemptive treatment was used for CMV prevention. 168 D+R− KTR were included between 2003 and 2011, 40 with l-od, 36 with e-od and 92 without disease. 87.5% of l-od occurred after universal prophylaxis whereas 89% of e-od occurred after preemptive strategy ($\chi 2$; $p < 0.0001$). Compared to patients with e-od, patients with l-od had significantly less recurrences (Odd Ratio = 0.2; 95% CI = 0.08-0.5; $p = 0.001$). Furthermore, when we compared the outcomes at 3 year post-transplantation of KTR with respectively l-od, e-od and no disease, the incidence of biopsy-proven acute rejection (30% vs. 18% vs. 25%, $p = 0.6$), graft survival (90% vs. 82% vs. 93%, $p = 0.2$) and patient survival (95% vs. 100% vs. 100%, $p = 0.06$) were not significantly different. In D+R− KTR, universal prophylaxis is associated with late-onset disease that has better infection outcomes, and has no detrimental effect on graft and patient outcomes at 3 year post transplantation. These results support the use of a universal prophylaxis over a preemptive strategy in D+R− KTR.

BO73 VALIDATION OF THE SUITABILITY OF A NOVEL ELISPOT ASSAY TO ASSESS THE FUNCTIONALITY OF CELL-MEDIATED IMMUNITY (CMI) IN HEMODIALYSIS PATIENTS

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Objective: Impairment of cytomegalovirus (CMV)-specific cell-mediated immunity (CMI) by immunosuppressive therapy is a major cause for CMV reactivations and associated complications in solid organ transplantation. Assessing the function of CMV-specific CMI may help to individually adjust immunosuppressive as well as antiviral therapy. The novel (T-Track® CMV) allows the simultaneous detection of CMV- reactive T-helper- and cytotoxic T-cells as well as NK- and NKT-cells using T-activated pp65 and IE-1 proteins for in-vitro restimulation of PBMC and an IFN-γ ELISpot assay. The aim of this study was to evaluate the suitability of the novel tool T-Track® CMV for assessing the CMV-specific CMI in a clinically relevant pre-transplant patient population.

Methods: Sensitivity and specificity of T-Track® CMV were examined in a cohort of 124 hemodialysis patients of whom 67 (54%) revealed a CMV positive serostatus. Moreover the results of (T-Track® CMV) were compared with (Quantiferon®-CMV) and a cocktail of 6 preselected CMV tetramers as reference tests.

Results: Herein, positive (T-Track® CMV) results were obtained in 60/67 (sensitivity 89.6%) of CMV- seropositive hemodialysis patients. Low, numbers of IE-1- but not pp65- reactive cells were observed in 12 of 57 CMV-seronegative dialysis patients confirming data showing IE-1 specific T-cell responses in seronegative individuals. For comparison, the reference tests (Quantiferon®-CMV) and CMV tetramer cocktail revealed sensitivities of 72.6% (45/62) and 76.9% (40/52), respectively.

Conclusion: (T-Track® CMV) can be used in a broad population of patients independent of their HLA-type. Thus, the assay may be a valuable tool to guide personalized antiviral and immunosuppressive therapy. Ongoing multicenter studies in renal transplant patients are supposed to reveal a threshold level of reactive cells that protects from uncontrolled CMV replication and related complications.

BO74 PRETRANSPLANT HEPATITIS B VIRAL INFECTION INCREASED RISK OF DEATH AFTER KIDNEY TRANSPLANTATION

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Background: Clinical outcomes have not been well evaluated in kidney transplant recipients (KTRs) with hepatitis B virus (HBV). Here, we aimed to investigate the recent posttransplant clinical outcomes in an HBV endemic country.

Methods: Among 4897 Korean kidney recipients from Aril 1999 to December 2011, 4412 patients whose viral hepatitis serology data was available were enrolled. Numbers of patients with HBV and hepatitis C virus (HCV) were 209 (4.7%) and 83 (1.9%).We analyzed the clinical outcomes, including overall mortality, graft failure, and new-onset diabetes after transplantation (NODAT), among patients who had taken kidney transplantation.

Results: Patients with HBV showed poorer survival than KTRs without HBV or HCV ($p = 0.004$, HR = 2.084, 95% CI 1.266–3.430). However HCV did not affect patient survival ($p = 0.119$, HR = 1.914, 95% CI 0.846–4.327). Patients with chronic hepatitis C showed increased incidence of graft failure ($p < 0.001$, HR = 2.271, 95% CI 1.481–3.480). However, the graft survival of patients with chronic hepatitis B was not different ($p = 0.773$, HR = 1.082, 95% CI 0.634–1.846). Incidence of NODAT was not increased in patients with chronic hepatitis B ($p = 0.493$, OR 1.180, 95% CI 0.734–1.897), but increased in patients with chronic hepatitis C ($p = 0.041$, OR 1.993, 95% CI 1.027–3.869). Among causes of patient mortality in chronic hepatitis B, hepatic causes were more prominent (1 hepatic failure, 2 hepatocellular carcinoma; 20.0% vs. 0.8%, $p < 0.001$) compared with patients without chronic hepatitis B. Patients with chronic hepatitis C and allograft failure showed increased trend of transplant rejection (83.3% vs. 68.6%, $p = 0.462$), but the statistical significance was not proved.

Conclusion: Kidney transplantation recipients with chronic hepatitis B could show poor survival due to post transplantation hepatic complications.

BO75 COMPARISON OF EFFICACY BETWEEN ENTECAVIR AND LUMIVUDINE ON HEPATITIS B VIRUS CARRIERS AFTER KIDNEY TRANSPLANTATION

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Objective: To compare the efficacy between entecavir and lamivudine as prophylactic antivirus therapy on long-term outcomes of HBV carriers after kidney transplantation.
Methods: We retrospectively reviewed HBV carriers with HBsAg-positive before kidney transplantation performed in our hospital from February, 2006 to December, 2012. All recipients were HBV-DNA negative before transplantation. 65 HBV carriers received entecavir as prophylactic antivirus therapy after kidney transplantation, and these patients were matched by 130 HBV carriers who received lamivudine based on HBeAg status and age. The patients were followed up, and HBV-DNA was detected every 3 months or when serum aminotransferases were abnormal. The primary endpoints were HBV reactivation (HBV-DNA transferring to positive), graft loss or patient death. Hepatic dysfunction, hepatic failure and hepatocellular carcinoma were also recorded.
Results: Patients received entecavir could significantly reduce HBV reactivation rate after kidney transplantation compared to lamivudine (9.2% vs. 20.8%, $p = 0.043$). In patients with HBeAg-positive, HBV reactivation rate was 3/15(20%) in entecavir group versus 16/30(53.3%) in lamivudine group ($p = 0.033$). Entecavir could also reduce the incidences of hepatic dysfunction (33.8% vs. 49.2%, $p = 0.041$). Hepatic failure (1.5% vs. 3.8%, $p = 0.66$) and hepatocellular carcinoma rate were comparable between two groups (1.5% vs. 4.6%, $p = 0.276$). Kaplan-Meier analysis showed that long-term patient and graft survival were also comparable between the two groups.
Conclusion: Compared to lamivudine, entecavir may reduce HBV reactivation and hepatic dysfunction in HBV carriers after kidney transplantation, however patient and graft survival were comparable.

BO76 *MYCOBACTERIUM TUBERCULOSIS* IN SOLID ORGAN TRANSPLANTATION, IMPACT OF EXPANDED ISONIAZID PROPHYLAXIS

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Background: Tuberculosis is a major challenge in solid organ transplantation, with increased risk of activation, complications, and mortality. We report frequency and incidence of Mycobacterium tuberculosis infection in transplant recipients and the results of expanded isoniazid chemoprophylaxis.
Methods: Recipients of solid organ transplantation during a 10-year period (January 2003-December 2012) are included. Tuberculosis-free transplantation follow-up is used for incidence rates calculation. The impact of expanded isoniazid chemoprophylaxis in renal transplant recipients on tuberculosis rates is reported.
Results: Of 1966 solid organ transplantation recipients as kidney (1391), liver (426), heart (114), and lung (35), 20 recipients (1.02%) developed tuberculosis. Incidence is 2.48 cases per 1000 transplant-years. Twelve cases (60%) developed tuberculosis within 1 year of transplantation. The frequency and incidence of tuberculosis per 1000 transplant-years for specific organs are: kidney: 0.58% and 1.27, liver: 1.88% and 5.94, heart: 1.75% and 5.7, and lung: 5.71% and 47.5. On survival analysis, only lung transplant recipients had significant difference compared to recipients of kidney from living donor (p value 0.0001), rate ratio 45.3 times (95% CI: 7–313). Case fatality was 5%. Fourteen patients (70%) were cured without any documented relapse. Two transplanted kidneys were lost. After the expanded isoniazid chemoprophylaxis among deceased-donor kidney recipients, no tuberculosis occurred in 177 recipients, compared to 3 out of 155 (2%) recipients before the program.
Conclusions: Tuberculosis among our solid transplant recipient population is reduced. The expanded isoniazid chemoprophylaxis among renal transplant recipients resulted in reduction of tuberculosis.

BO77* AN EXPECTANT REDUCTION IN IMMUNOSUPPRESSION IS AN EFFECTIVE MEANS OF REDUCING THE INDICENCE OF GRAFT FAILURE IN RENAL TRANSPLANT RECIPIENTS WITH BK NEPHROPATHY

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Background: BK virus reactivation, diagnostic for graft nephropathy, is found in up to 10% of renal transplant recipients, of which graft failure is observed in 15% or more. No effective pharmacological therapies exist and treatment is a tailored reduction in immunosuppression. Viral screening is vital in early detection so that expectant measures are taken to avoid graft failure. We present a review of our BK screening programme.
Methods: A 2-year retrospective analysis was undertaken of recipients undergoing renal transplant at the Royal Liverpool University Hospital in 2011 and 2012. Significant BK viraemia is taken as an absolute copy number of 10 000 per ml.
Results: Of 201 transplants, 49 patients had BK viraemia but only 19 (9.4%) developed significant viraemia (these are the BK positive group). Onset of viraemia was most frequently observed 3–9 months post-transplant. Deceased donor grafts, male recipients, diabetic recipients and higher numbers of HLA-mismatches were not significantly more frequent in the BK positive group. However, induction with Alemtuzumab was seen in 84.2% of the BK positive group compared to 54.4% in the BK negative group ($p = 0.01$).All patients were treated with a tailored reduction in immunosuppression; one patient with persistent viraemia received oral fluoroquinolone. In the BK positive group, 1 patient (5.3%) experienced graft failure compared to 6 (3.3%) in the BK negative group ($p = 0.50$). Graft nephrectomy and patient mortality rates were similar.
Conclusion: The majority of significant BK viraemia occurs within the first year post-transplant and those receiving Alemtuzumab, are most at risk. Good clinical outcomes are observed with an expectant reduction in maintenance immunosuppression. A regular screening programme in the early post-transplant phase is fundamental to maximising preservation of graft function, reflected in our experience of only 5% graft failure, compared to upwards of 15% quoted in the literature.

BO78 PRETRANSPLANT RITUXIMAB PREVENTS EBV TRANSMISSION IN EBV-SERONEGATIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: Due to a striking increase in the risk of posttransplant lymphoproliferative disorder in EBV-seronegative kidney transplant recipients (KTRs) receiving an allograft from an EBV-seropositive donor, special strategies need to be defined to prevent EBV transmission and EBV replication.
Methods: Here, we studied all kidney transplant recipients (KTRs) at our single transplant center transplanted between 2008 and 2012. 17 of 402 KTRs (4.2%) were identified as EBV-seronegative recipients from an EBV-seropositive donor, among which 5 KTRs received kidneys from living donors and 12 KTRs received kidneys from deceased donors. KTRs undergoing living kidney donation were treated with a single dose of rituximab 4 weeks prior to renal transplantation. Assessment of EBV-seroconversion and EBV viremia were performed in follow-up in all KTRs.
Results: Among the 12 EBV-seronegative KTRs from deceased donors, all 12 KTRs (100%) showed EBV-seroconversion, 7 KTRs (58%) showed active EBV-viremia, and 2 KTRs (17%) showed development of posttransplant lymphoproliferative disorder. In comparison all 5 KTRs from living donors, who received pretransplant rituximab, remained EBV-seronegative after renal transplantation, without EBV viremia or posttransplant lymphoproliferative disorder in follow-up ($p < 0.05$). All KTRs, who received pretransplant rituximab, show excellent allograft function, no increase in infectious complications or malignancies.
Discussion: Our data suggest that rituximab-mediated elimination of B-cells prevents transmission of EBV to the recipient, since EBV persistence requires the establishment of a latent infection in recipient B-cells. Pretransplant rituximab may proof useful to prevent primary EBV-infection in EBV-seronegative KTRs undergoing living kidney donation.

BO79 THE ROLE OF ANTIFUNGAL THERAPY IN SMALL BOWEL TRANSPLANTATION: A SINGLE CENTRE 5-YEAR EXPERIENCE

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Background: Small bowel transplantation is the treatment of choice for a select group of patients that fulfill the criteria set out by the American Gastroenterology Association. Although immunosuppressive therapies have evolved over the years, the transplant recipients overall immunosuppressed status predisposes them to infectious complications. Depending on the organ transplanted, the incidence of invasive mycoses ranges from 5 to 42%. Candida and Aspergillus spp. produce most of these mycoses. In this study, we assessed the incidence of invasive aspergillosis after SBT and the role, safety and peculiar side effects of antifungal prophylaxis in small bowel transplant patients over a period of 5-years.
Methods/Materials: We retrospectively investigated from October 2008 to date, 32 SBT's have been done at the Oxford University Hospitals Transplant Centre.
Results: There were 9 sustained episodes of neutropenia in the last 5 years. The first 2 patients with neutropenia did not get any antifungal prophylaxis during the episode of neutropenia. These two patients died from an invasive aspergillus abscess in the brain. The unit policy was changed at this point to include antifungal prophylaxis in patients having sustained neutropenia and thus the second phase was defined. Since the Institution of the 'second phase' of anti-fungal delivery, there has been no more incidence of invasive aspergillus infection.
Conclusion: Institution of antifungal prophylaxis during neutropenic periods was adopted for all patients post SBT with sustained neutropenia. This we believe may be one of the reasons that we have not seen any more invasive aspergillus infections. Antifungal prophylaxis is generally safe in small bowel transplant patients.

BO80 PREVALENCE OF HUMAN HERPES VIRUS 6 GENOME IN BLOOD SAMPLES FROM PEDIATRIC AND YOUNG ADULT KIDNEY TRANSPLANT RECIPIENTS

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Background: Human herpesvirus 6A (HHV6A) and 6B (HHV6B) are distinct species belonging to the Roseolovirus genus. HHV6 is considered an ubiquitous virus and its worldwide sero-prevalence is approaching 100%. After the primary infection, HHV6 establishes latency in the host, mainly in peripheral blood monocytes (PBMCS) and may reactivate under immunosuppression conditions, such as transplantation. The presence of HHV6A/B genomes and its replication were investigated in blood samples collected from pediatric and young adult kidney transplant recipients.
Materials and Methods: Peripheral blood samples were obtained from 55 pediatric (men age: 17.0 years) and 22 young adult patients (mean age: 29.7 years). The mean time from transplant was 74.8 months (range: 1–258 months). PBMCS and plasma were separated from blood and viral DNA was extracted. Polymerase Chain Reaction real time assay (q-PCR), targeting U67 region, was employed for the quantification of HHV6 genome in PBMCS. A nested PCR assay, able to differentiate HHV6A from HHV6B, was carried out. To discriminate the active replicating virus, both the presence of viral DNA in plasma samples and of the U100 and U67 transcripts in blood samples were analyzed by means of specific q-PCR and one step-reverse transcriptase PCR assays (RT-PCR), respectively.
Results: The viral genome was detected in 16/77 patients (20.8%), with a mean viral load of 788.4 copies/ml (range: 61-1800 copies/ml). Ten out of 16 (62.5%) HHV6 positive patients were infected with the HHV6A. The viral genome was not detected in any of the tested clinical specimens, whereas the U100 and U67 transcripts were detected in one blood sample. No significant association was observed between the HHV6 infection, the patient's age, the time passed from the transplant, the HCMV co-infection and the clinical sympto. Conclusion

HHV6 infection, even if frequently detected, seems not be associated with post transplant disorders in kidney transplant recipients.

023 KIDNEY

BO82 INTERLEUKIN-17-DEPENDENT IL-23 PLASMA LEVEL IS STRONGLY ASSOCIATED WITH CMV STATUS IN PATIENTS WITH END STAGE RENAL DISEASES

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Cytomegalovirus (CMV) seropositivity is an unexpectedly high and independent risk factor for atherosclerosis in patients with ESRD. Without anti-CMV therapy, donor CMV seropositivity is a detrimental factor for long-term renal allograft survival. Human Th17 pro-inflammatory cells are currently defined as cells that produce IL-17, tumor necrosis factor (TNF)-α, IL-6, IL-9, IL-21, IL-22 and IL-23 and thought to be involved in rejection after organ transplantation. Latent CMV infection induces Th17 lymphocytes which might be involved in the pathogenesis of CMV seropositivity in patients with ESRD.

We aimed to evaluate associations of Th17-dependent cytokines with ESRD and CMV seropositivity in potential kidney transplant recipients. Pre-transplant plasma levels of IL-9, IL-21 and IL-23 in 117 consecutive potential kidney transplant recipients and 27 healthy controls (HCs) were analyzed.

Plasma levels of IL-9 ($p = 0.64$) and IL-21 ($p = 0.66$) were similar in patients with ESRD and HCs, whereas the plasma level of IL-23 was significantly higher in patients with ESRD ($p < 0.0001$) (Figure 1). CMV-seronegative ($p = 0.004$) and –seropositive ($p < 0.0001$) ESRD patients had significantly higher IL-23 plasma levels than HCs (Figure 2). Interestingly, compared to CMV-seronegative patients CMV-seropositive patients showed significantly higher IL-23 ($p = 0.001$) plasma levels.

Our results indicate that latent CMV induces Th-17. TH-17-dependent IL-23 might be an inflammatory response to latent CMV infection which increases risk of atherosclerosis in patients with ESRD and might damage the allograft.

BO83 USE OF CONTRAST-ENHANCED ULTRASONOGRAPHY TO EVALUATE RAT CHRONIC ALLOGRAFT NEPHROPATHY AND CORRELATIONS BETWEEN TIME-INTENSITY CURVE PARAMETERS AND ALLOGRAFT FIBROSIS

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Objectives: To quantitatively analyze the changes of hemodynamic characteristics in renal allograft at different stages of a rat chronic allograft nephropathy (CAN) model and the relationship between hemodynamic parameters and renal allograft fibrosis using contrast-enhanced ultrasonography (CEUS) technique

Methods: The experimental group used a CAN rat model ($n = 30$). The control group used orthotopic syngeneic renal transplant model ($n = 30$). After the surgery, creatinine clearance rate was regularly monitored. At 4, 12, and 24 weeks after surgery, 8 rats from each group were randomly selected for CEUS examination. Parameters related to time intensity curve (TIC) were determined. At the same time, chronic allograft damage index (CADI) scores was used to evaluate each group of renal allograft specimens. Immunofluorescence and Western blot were used to measure α- smooth muscle actin (α-SMA) and Vimentin expression in renal allograft tissue and the correlation between the expression levels and the TIC curve parameters was analyzed.

Results: Before the conventional indicator, creatinine clearance rate, for the evaluation of renal allograft function, showed significant abnormality, the renal allografts in the experimental group had already presented CAN pathological changes. At the early stage after the surgery, as compared to the TIC curve of the control group, the experimental group showed delayed contrast enhancement. CADI score and the expression levels of α-SMA and vimentin proteins in renal allograft were correlated with TIC parameters

Conclusion: Compared to creatinine clearance rate, CEUS can detect CAN at earlier stages. The correlation between TIC-related parameters and the expression levels of α-SMA and vimentin proteins in renal allograft indicates that CEUS can quantitatively measure microcirculation perfusion in renal allograft, thus quantitatively assessing the degree of renal allograft fibrosis.

BO84 INTRA-OPERATIVE USE OF IMPLANTABLE DOPPLER PROBES COULD POTENTIALLY REDUCE RENAL GRAFT LOSS FROM VASCULAR COMPLICATIONS

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Introduction: Renal vessel thrombosis is a common cause of early graft loss. Conventional ultrasound scanning (US) does not allow continuous monitoring, therefore, significant diagnostic delays are inevitable. An implantable doppler probe (IMDP) placed onto the renal artery would allow continuous monitoring, potentially, allowing more expedient intervention. We looked at our own series of patients with an IMDP.

Methods: We retrospectively reviwed prospectively collected data of consecutive renal transplants that had IMDP from April 2011 until October 2014 within our institution.

Results: 110 patients with a median age of 52.5 years were identified. Overall 20 (18.2%) patients were re-explored and 14 (12.7%) of these were re-explored due to an abnormal IMDP signal.

Of these 14 patients four (3.6%) returned to theatre during the post-operative period and ten (9.1%) were re-explored while still in theatre. Two of those who returned to theatre required revision of the vascular anastomoses and one of these patients also required mesh closure to maintain perfusion. In the third patient the renal graft was re-explored promptly and the kidney was normal, but 24 h later the graft was ischemic due to renal vein thrombosis. The fourth patient had a normal kidney on re-exploration.

Of the ten patients who were re-explored while still in theatre six (5.5%) required revision of both vascular anastomoses. Mesh closure was performed in five (4.5%) patients to increase the space.

Discussion: Detecting thrombotic complications after transplantation relies on clinical changes and US, which may lead to diagnostic delay. In this series the IMDP has probably improved outcome in 12 (10.9%) patients. In all these cases the problem was identified sooner than clinical assessment and US alone, indeed ten problems were identified while the patient was still in theatre. In conclusion, IMDPs may allow early diagnosis allowing prompt graft saving treatment and we can recommend their use.

BO85 GENE EXPRESSION IN THE DECEASED DONOR KIDNEY DETERMINATES ALLOGRAFT FUNCTION

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The donor brain death is one of the most important factors influencing the outcome of kidney transplantation. In this study we assessed the effect of donor brain death on allograft function, as well as intragraft gene expression of 28 genes involved in immune response. Material and Methods

The core biopsies were obtained from 76 kidneys of 43 deceased donors during organ retrieval, before flushing with cold solution. 12 biopsies from living donors during transplantation served as a controls. Gene expression levels were determined on low-density arrays (32-format, Taqman).

Results: Expression of genes connected to tissue injury pattern (LCN2, TLR2, HMGB1, NOS2, NFKB1, MMP9, GUSB, CSF1), lymphocyte activation (IL2, FAS), inflammation (IL6,TNF), cell migration (IL8, CD68, CCL2) and apoptosis (CASP3, TP53) were significantly up-regulated in donor kidneys, which subsequently presented delayed graft function and/or acute rejection episode, compared to event free individuals. Moreover the 1-month allograft function correlated significantly with expression of tissue injury related genes (LCN2, NFKB), lymphocyte activation (IL2, FAS), inflammation (IL6, TNF), cell migration (IL8, CCL2) and apoptosis-related genes (CASP3, TP53). The impact of donor up-regulation of three genes (IL6, IL8, LCN2) on kidney function was observed up to 6 months. From the clinical factors only donor age influenced negatively short as well as long-term allograft function. Better quality of kidneys retrieved from multiorgan procurement resulted in lower rate of delayed graft function and better function up to 12 months post transplantation.

Conclusion: Our data show that the increase in expression of pro-inflammatory, tissue injury- and apoptosis-related genes observed in the kidneys from deceased donors are the hallmarks of the initiated organ injury process. LCN2, IL6 and IL8 expression level in the retrieved kidneys were significant determinants of their post-transplant function.

BO86 RNA PROFILING OF URINARY EXTRACELLULAR VESICLES (EV) IDENTIFIES ACUTE REJECTION IN KIDNEY TRANSPLANTATION

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T cell and Anti-Body mediated rejection (TCMR and ABMR) are leading cause of loss of kidney transplant (KT) function. Several biomarkers have been proposed for diagnosis, however, graft biopsy is still necessary in the clinical practice. Urinary extracellular vesicles (EV) may be accurate biomarkers of rejection. EV are nanoparticles involved in cell-to-cell communication able to shuttle proteins, lipids and nucleic. The aim of the study was to evaluate RNA profiling of urinary EV of KT patients to identify TCMR and AB.Urine of 69 patients admitted for performing graft biopsy were collected. EV concentration and size were evaluated by nanoparticle tracking analysis (Nanosight, UK). Plasma NGAL was also evaluated (Alere, USA). mRNA profiling of urine EV was performed in all biopsy-patients, in 12 patients with stable graft function and 14 healthy control by collection devices. Identified genes were analyzed by literature screening via web platform (ProteinQues,t Biodigital Valley, ITA) to find associated miRNA.Nanosight analysis showed a significant decrease of EV concentration and size in TCMR not observed in other causes of functional impairment ($p < 0.05$). NGAL levels were significantly higher in TCMR than in other KT subjected to biopsy ($p < 0.0002$). EV gene profiling showed that renal mRNA (i.e. SLC12A1, UMOD, AQP2) and other mRNA (i.e. ACTB, ALB) were significantly altered in graft rejection ($p < 0.005$). Logistic regression analysis of mRNA distinguished TCMR and ABMR from other causes of functional impairment (AUC 0.940 and 0.730). By ProteinQuest, we found 5 miRNA (miR-10a, miR-142, miR-192, miR-30a and miR-let7c) associated with rejection in literature or with mRNA down-regulated in our patients. Preliminary data suggested an increase of the identified miRNA in EV. In conclusion, evaluation of urinary EV concentration, size and mRNA profiling may allow accurate and noninvasive diagnosis of rejection. NGAL may further improve diagnostic accuracy.

BO87 THE ASSOCIATION OF DELAYED KIDNEY GRAFT FUNCTION WITH A CONSTANTLY VERY LOW EXPRESSION OF THE MESSENGER RNA TLRS2-4,9 FROM PERIPHERAL BLOOD MONONUCLEAR CELLS OF THE RECIPIENT

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Background: The Toll-like receptors (TLR) 2–4.9 are engaged in the pathogenesis of acute renal injury. Andrade-Oliveira V (Transplantation. 2012 Sep 27;94(6):589–95) demonstrated that 24 h after transplantation, the expression of the messenger RNA (mRNA) TLR4 of peripheral blood mononuclear cells (PBMC) from patients (pts) with delayed graft function (DGF) was lower than in recipients of kidneys which started the work immediately. The aim of study was to examine whether the reduced expression of TLR2-4,9 mRNA is a long-lasting phenomenon associated with DGF.
Material and Method: Each of the 151 transplant patients was more than 1 month after transplantation (from 1 to 128 months). Within this group: in 117 patients blood sample was taken for more than 3 months after transplantation, 45 patients experienced delayed graft function. TLR2-4,9 mRNA from PBMC was assessed by polymerase chain reaction (real-time PCR) and analyzed in terms of DGF and clinical course.
Results: We found a clear negative correlation between the expression of TLR2-4,9 mRNA and duration of DGF. Kidney recipients who developed DGF had generally lower TLR2-4,9 mRNA expression than patients without DGF (TLR2: $p = 0.06$; TLR3; $p = 0.021$; TLR4: $p = 0.07$; TLR 9, $p = 0.027$) In multiple regression analysis low expression of TLR mRNA 2-4,9 was associated with the occurrence of DGF in the past. The differences become more pronounced in the patients examined more than 3 months after transplantation.
Conclusion: Very low mRNA expression of TLRs 2-4,9 seems to be a permanent feature of peripheral blood mononuclear cells in the recipient of the transplanted kidney, which increases the risk of delayed graft function. TLR2-4,9 mRNA expression could potentially be used as an indicator of the likelihood of delayed graft function.

BO88 MARKERS OF KIDNEY INJURY AFTER DECEASED DONOR KIDNEY TRANSPLANTATION

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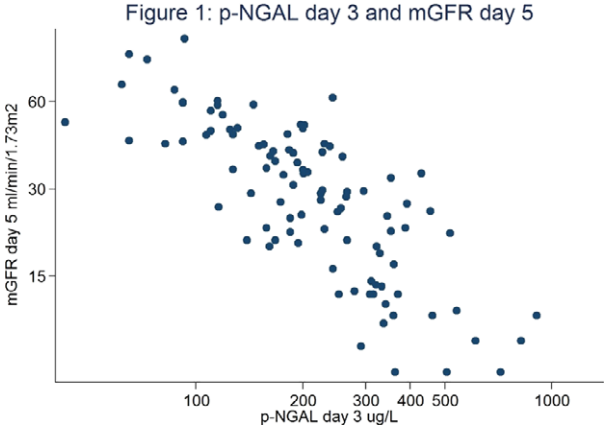
Background: Delayed graft function (DGF) after deceased donor kidney transplantation is common. It is associated with greater risk of complications, prolonged admission and post-transplant dialysis. Biomarkers that predict early graft dysfunction can facilitate interventional studies. This study focus on early graft function and evaluates the association with liver-type fatty acid-binding protein (L-FABP), Cystatin C, YKL-40, and neutrophil gelatinase associated lipocalin (NGAL).
Methods: Blood and urine sampling was carried out as part of a randomized, controlled, multicentre study. In total 222 recipients of a deceased donor kidney transplant were included. YKL-40 and L-FABP were analysed using ELISA, and NGAL and Cystatin C using commercially available automated assays. All renal biomarkers were analysed in urine at baseline, 90 min after reperfusion, at day 1 and 3 postoperatively. NGAL was also analysed in plasma. The results were correlated with the time until a 50% reduction in P-creatinine and measured GFR (^{51}Cr-EDTA) 5 days after transplantation.
Results: Our data show a correlation between plasma NGAL levels on both day 1 and 3 postoperatively and measured GFR on day 5 (figure 1).

Figure 1: p-NGAL day 3 and mGFR day 5



Conclusion: NGAL in plasma predicts GFR at day 5 after deceased donor transplantation. Additional analyses on our data will clarify whether combinations of biomarkers, plasma creatinine and urinary output are superior to the two latter alone in prediction of early graft function.

BO89 EFFECTS OF EXTRACORPOREAL PHOTOPHERESIS (ECP) ON ELISPOT AND DENDRITIC CELLS PHENOTYPE IN KIDNEY ALLOGRAFT RECIPIENTS

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Objective: To study cellular alloimmunity and dendritic cells (DCs) phenotype (mature/immature) in kidney allograft recipients who underwent ECP procedures.
Material and Methods: Cadaver KTx in 20 paired recipients, all of them on standard immunosuppression (MPA+CNI+prednisone), and 10 of them additionally treated with 12–16 ECP procedures in the first 3 months (M) following KTx. ECP procedures were conducted using UVAR XTS (Therakos, Exton, PA), an automated system for leukocyte separation and photoactivation (with injection of Methoxsalen). All pts were followed by means of eGFR and peripheral WBCs, DCs counts and phenotype (BDCA1,3).Cellular alloimmunity was studied before transplantation (day 0) and 3, 12–24 months post KTx using an interferon-gamma enzyme-linked immunosorbent spot assay(ELISPOT). For ELISPOT data analysis results (spot number, size) were recalculated as the ratio of the values observed for donor-stimulated to unstimulated recipient cells corrected for residual donor activity.
Results: In ECP group a positive tendency to higher GFR at M3 (67.5 vs. 53.6; $p = 0.03$) and M 12 (64.4 vs. 59.53 $p = 0.09$ in Wilcoxon test) was observed. Significantly greater donor-stimulated activity (ELISPOT) was observed in recipients who underwent ECP when measures were obtained after completing ECP procedures at M3 comparing to M12-24 – mean change in spot size was 4.2 vs. 1.8 ($p < 0.05$). In the control group (paired without ECP) mean change in spot size was 1.5 vs. 0.8 ($p < 0.05$) at M3 and M12-24 respectively. In ECP group more myeloid DCs (BDCA1,3) were immature than

in controls at M3 (87% vs. 67% and 87% vs. 70%, p = 0.05; BDCA1 and 3 respectively).
Conclusion: Favorable kidney function at M3 was associated with more immature phenotype of DCs and transiently greater cellular alloimmunity as measured with ELISPOT.

BO90 RELEVANCE OF RENAL ALLOGRAFTS CALCIFICATIONS DETECTED BY PROTOCOL BIOPSIES

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Renal allograft calcifications have been reported in different studies, however, the etiology, risk factors and prognostic significance of this finding for the graft are unclear. The aim of this study was to determine the prevalence and risk factors of calcium-phosphate deposits in renal grafts and see whether calcification is related to disturbed mineral metabolism and contributes to graft dysfunction at 1 year after transplantation.

Single-centre retrospective observational study including 188 renal transplants patients at our hospital between 2009 and 2011. We performed kidney protocol biopsies at 3 and 12 months. We evaluated demographic data, immunosuppression and biomarkers of mineral metabolism (calcium, phosphorus, i-PTH, alkaline phosphatase (AP), 25 Vitamine D) and renal function at 3 and 12 months.

Calcifications were observed in 35.6% of the patients at 3 months. At 12 months 9% persisted and 13% were de novo calcifications. The 54.1% of patient who had received an expanded criteria donors allograft presented calcifications vs. 23.6% who received a standard allograft (p 0.003). The patients presenting acute tubular necrosis post transplant 34.3% presented calcifications vs. 16.5% who did no (p 0.045). At 3 months calcium, i-PTH and AP were significant higher in calcification group (calcium 9.89 $\pm$ 0.60 mg/dl vs. 10.34 $\pm$ 0.86 mg/dl (p = 0.045), i-PTH 160.0 (123.0 – 191.7) pg/ml vs. 333.0 (194.0 – 736.0) pg/ml (p = 0.020), AP 217.00 $\pm$ 95.14 UI/l vs. 263.89 $\pm$ 100.52 UI/l (p = 0.045). We do not observe differences at 12 months between groups. Renal function after a year follow-up was similar in patients with and without calcifications (Creatinine 1.57 $\pm$ 1.07 mg/dl vs. 1.47 $\pm$ 0.84 mg/dl (p = 0.958)).

Renal graft's calcifications are a frequent finding and seem to be associated with donor subtype, acute tubular necrosis and alterations in mineral metabolism. No statistically significant differences in renal function at 1 year of follow-up were observed.

027 LUNG

BO91 EARLY REPORT OF A CLINICAL TRIAL DESIGNED TO PROCURE LUNGS FROM UNCONTROLLED DCD DONORS

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Objective: We present and early report of a clinical trial designed to procure lungs from uncontrolled DCD donors (NCT02061462).
Methods: According to our protocol, subjects with cardiovascular collapse, initially treated in-loco, then trasfered to the emergency room (Ospedale San Gerardo, Monza), are considered as potential uncontrolled-DCD donors if declared dead after worthless ECLS. Unwitnessed collapse, no flow period of >15 min, low flow >60 min are exclusion criteria. After clinical diagnosis of death (5 min of no touch), continuous positive end-expiratory pressure (CPAP 10 cmH2O, 100% FiO2) is applied until death is confirmed according to circulatory criteria (20 min of flat EKG by law in Italy), and consent to donation obtained. Thereafter, heparin is given (10 000U ev push, followed by 3 min of CPR), and low frequency-low tidal volume-high PEEP ventilation is started. If chest X-ray and broncoscopy are negative, the subject is transfered to the OR, lungs are perfused with fibrinolitic agents (15 mg rTPA), flushed with preservation solution (60 ml/Kg antegrade, 250 ml retrograde), and cold stored on ice. Lung function is then evaluated after 4 h of EVLP reconditioning (Fondazione Ca' Granda – 25 km distant form Monza).
Results: Six potential donors were evaluated over a 6 month period; one was recruited on November 1st, 2014. He was a 46 year old male who died with aortic dissection (0 min no flow, 43 min low flow). Consent to donation was obtained 2 h later. Lungs were procured 4 h and 23 min after death, deemed suitable after EVLP, and offered to a recipient with cistic fibrosis (LAS 46) who consented to the investigation. Lung function was proper throughout ICU (19 days) and hospital (39 days) stay. Three months after transplantation the recipient is well being (FEV1 85%).
Conclusions: We have shown that lung procurement from category II DCD donor is feasible even after an extended period of warm ischemia.

BO92 NEUROGENIC PULMONARY EDEMA: EFFECT OF CORTICOSTEROIDS

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Introduction: In lung transplantation, neurogenic pulmonary edema (NPE) is a major impediment to lung harvesting. Corticosteroids may mitigate pulmonary edema but the role of inflammation in the pathogenesis of the condition remains uncertain.In a model of brain death (BD), we studied the role of inflammation in the NPE pathobiology.
Methods & Results: Sixteen pigs were randomized to placebo ($n = 9$) or corticosteroids ($n = 7$) 1.5 mg/kg before BD induced by slow intracranial blood infusion. Four hours after BD, the animals underwent a hemodynamic evaluation followed by lung tissue sampling for rtq-PCR for HO-1 and the pro-inflammatory ratio IL-6 / IL10, and lung histopathologic injury score. A control group ($n = 9$) was studied.BD increased pulmonary pressure (PAP), pulmonary vascular resistance (PVR), capillary pressure (Pcap), pulmonary arterial impedance at 0 Hz (Z0), and pulmonary arterial elastance (Ea). Systemic arterial pressure (SAP) was decreased while occluded pulmonary arterial pressure, right auricular pressure and characteristic impedance did not change. The ratio of partial pressure arterial oxygen and fraction of inspired oxygen (Pa02/Fi02) collapsed. BD was associated with an increase in IL-6/IL-10 and a decrease in HO-1 gene expression. The injury score was increased in BD group.Corticosteroids therapy totally prevented changes in PAP, PVR, Pcap, Z0, Ea, and IL6/IL10 and HO-1 gene expression in lung tissue. Changes in Pa02/iF02 and injury score were partially prevented.
Conclusions: BD is responsible for neurogenic pulmonary edema. Corticosteroids prevent hemodynamics and partially prevent biological changes in neurogenic pulmonary edema.

007 DONATION/RETRIEVAL

BO93

LUNG TRANSPLANT FROM DONOR AFTER CARDIAC DEATH (UDCD): THIRTEEN YEARS LATER

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Hospital Clinico San Carlos

Objective: Hospital Clínico San Carlos (HCSC) has developed a specific program to obtain organs and tissues from uDCD. Experience with kidneys and tissues is excellent. We developed a specific program to obtain also lungs.
Method: We modified uDCD inclusion criteria for lungs: 1-Age between 12-60. 2–Exclude bilateral thoracic trauma. 3- Initiation of CPR maneuvers <10 min. 4-Evaluation includes chest x-ray and examination of tracheal tube. We establish extracorporeal bypass with membrane oxygenation as uDCD general procedure, and initiate specific lung preservation maneuvres: 1-Obtaining of 300 cc of blood. 2-Placement of thorax drainage tubes and infusion into thorax through tubes of Perfadex® solution, 4 liters at 4°C in each hemithorax. 3- Wait until obtain family and judge permission. 4- Removal of Perfadex® from thorax and reinitiate ventilation. 5- Bronchoscopy. 6- Sternotomy 7-Pulmonary artery (PA) cannulation and right atrium drainage. 8-Add to the blood obtained (300 cc) PgE, introducing this solution through PA. 9-Obtain blood sample for gas determination from each pulmonary vein (PV). 10-After lung validation, cardiectomy and extraction of lungs and preservation.
Results: We performed the first lung transplant in November 2002. From there we have transplanted 103 lungs (92 bipulmonary and 11 unipulmonary) with uDCD. Longest time of survival is 13 years, and functional situation is excellent. Mortality at the hospital is 16%. Survival rates were 97% at 1st year, 83% at 3 years, and 73% at 5 years.
Conclusions: 1-Preliminary study showed the excellence of lungs for transplant prior to clinical experience. 2- Functional validation of lungs offers enough evidence to asses transplant.3-Maneuvers of preservation have proved to be very effective. 4- Lungs of uDCD have demonstrated good functional results. 5-Once uDCD program is developed it must be established an specific procedure to get the lungs.

027 LUNG

BO94 IMPACT OF TRANSFER PROCESS ON PA02/FIO2 RATIO IN BRAIN DEAD POTENTIAL DONORS AND EFFECT OF RECRUITMENT MANEUVER ON ITS REVERSAL: A CONTROLLED CLINICAL TRIAL

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Background: Organ donation system in Iran is based on transfer of donors to organ procurement units (OPU) of university hospitals for management. In this study we examined the impact of transfer process on donor's lungs quality indices such as PaO2/FIO2 ratio and effect of a single recruitment maneuver on its reversal.
Materials and Methods: In this two-phase controlled study we followed 52 brain dead donors during transfer and carefully followed the oxygenation criteria of their lungs. Three blood samples for arterial blood gases were collected immediately before and after transfer (T1 and T2) and 2 h after an alveolar recruitment maneuver for half donors (T3). We also obtained two arterial blood gas test results with the same time interval in control group (T1 and T2. Lung suitability criteria in blood gas sample for donation was a P/F ratio higher than 300.
Results: There were no differences in age, cause of brain death, intubation days, presence of chest trauma, chest tube and the amount of fluid administered during transfer in case and control groups. (Table.1) PaO2/FIO2 at T1 and T2 also were not statistically different in both groups. PaO2/FIO2 dropped significantly after transfer. (From 302.1 ± 119.4 to 259 ± 115.8 mmHg, $p < 0.001$) the transfer process turned 19.2% of all potential lung donors to inappropriate ones (5 in each group. The only influencing factor was the amount of IV-fluid administered during transfer period with a positive correlation with PaO2/FIO2 drop. ($p = 0.02$ and correlation coefficient = 0.540) The PaO2/FIO2 decrease from T1 to T3 was significantly lower in the recruitment maneuver group than in control group (−4.3 ± 44.1 vs. −69.5 ± 61.4 mmHg, $p < 0.001$).
Conclusions: Transfer of brain dead donors to OPUs is associated with a decrease in PaO2/FIO2 This can be significantly reversed by a single alveolar recruitment maneuver immediately after hemodynamic stabilization. Excess fluid administratio can exasperate the drop.

	Control group	Recruitment group	p-Value
Age	36.5 ± 15.7	37.3 ± 15.5	N.S
Sex (male)	55.7%	60.8%	N.S
Cause of B.D (trauma)	57%	61.5%	N.S
Intubation days	5.8 ± 6.2	6.5 ± 5	N.S
Smoking history (P.Y)	8 ± 10	6.5 ± 10	N.S
Mean arterial Blood pressure	92.2 mmHg	89.9 mmHg	N.S
Central Venous Pressure	12.7 ± 3.4	11.8 ± 3.1	N.S
PaO2/FIO2 (T1)	283.112.1	323.6 ± 126.5	N.S
PaO2/FIO2 (T2)	253.3 ± 125.6	267.3 ± 106	N.S
PaO2/FIO2 (T3)	230 ± 94.8	319.5 ± 133.2	0.017
PaO2/FIO2 (T2–T1)	33.2 ± 53	56.4 ± 58.5	N.S
PaO2/FIO2 (T3–T1)	−69.5 ± 61.4	−4.3 ± 44.1	>0.001

N.S = not significant.

BO95 FLUSH AND STORAGE TEMPERATURE INDEPENDENTLY AFFECT EPITHELIAL CELLS IN A RAT LUNG TRANSPLANT MODEL

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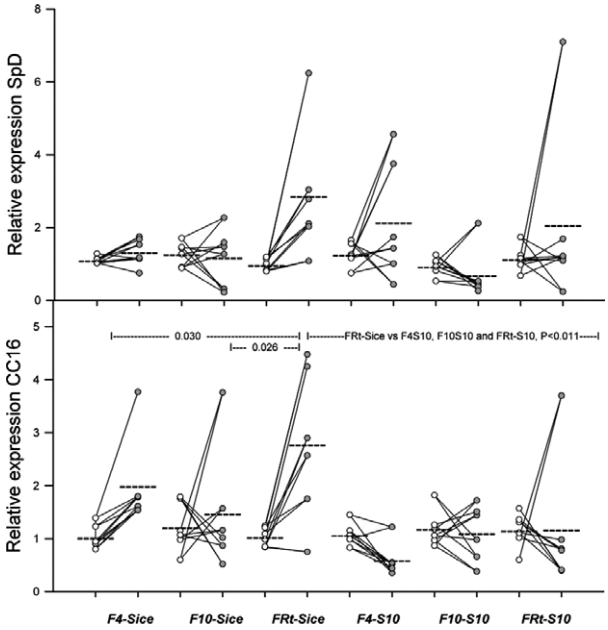
Ischemia/reperfusion injury is still not abandoned after lung transplantation. The extend of injury to epithelium after flush and storage may vary with temperature. This study investigates the effect of flush and/or storage temperatures on the change in epithelial cell specific gene expression after reperfusion in a rats.

Left donor lungs were transplanted after flushing at 4°C, 10°C or room temperature (F4/F10/FRt) in combination with storage on ice or at 10°C (Sice/S10) creating six experimental groups. Right donor lungs were flushed and stored but not transplanted. After 2 h reperfusion, genes involved in maintaining epithelial integrity were assessed in transplanted left lungs and compared to untransplanted right lungs.

We found that; 1. gene mRNA CC16 levels expressed by type I epithelium is solely affected by storage temperature. This led to a higher increase in gene expression after reperfusion in Sice lungs. 2. gene mRNA Sp-D levels expressed by type II epithelium was affected by flush temperature. Room temperature flush led to an increase of Sp-D expression after reperfusion, irrespective of storage.

Our results indicate that room temperature flush may have a preserving effect on type 2 epithelial cells and cold storage may preserve the integrity of type 1 epithelial cells.



Flush showed a main effect on SpD expression and storage showed a main effect on CC16 expression in perfused left (grey dots) compared to untransplanted right lungs (white dots). p-values; differences between groups, horizontal lines represent mean values.

BO96 INFLUENCE OF TREATMENT WITH HYPERTONIC SOLUTION BEFORE EVLP ON DONORS WITH HEMORRHAGIC SHOCK

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Pulmonary edema associated to hemorrhagic shock is one of the main reasons for donation refusal. Important advances have been achieved using the ex vivo perfusion methodology for organ reconditioning in an attempt to increase donor offer. However, the use of this technique in small animal models is still limited due to the progressive increase in pulmonary artery pressure and short perfusion period. Our hypothesis is based on a pre-treatment with hypertonic saline solution in donors with in vivo hemorrhagic shock associated to ex vivo lung perfusion. Sixty rats were divided in 3 groups: Shock (SH $n = 20$); Sham (S $n = 20$) and Hypertonic Solution (HS $n = 20$). After anesthesia the animals were submitted to femoral artery and vein catheterization for mean arterial pressure (MAP). MAP were monitored in the S group. Hemorrhagic shock was induced (40 mmHg) in the SH and HS groups and treatment with hypertonic solution at 4 ml/kg was adminitered to the HS group. After 120 min, 10 cardiopulmonary blocks from each group were forwarded to the Havard Apparatus IL-Isolated Perfused ex vivo perfusion system and were evaluated for 60 min. The other 10 blocks from each group were used for TNF-alpha cytokine dosing and neutrophil quantification. Treatment with hypertonic solution decreased TNF-alpha levels and the area of neutrophilic infiltrate in the SH group ($p \leq 0.001$). When the groups undergoing EVLP are compared to the ones without EVLP we observed an increase in neutrophilic infiltrate after perfusion ($p = 0.04$). As expected, the groups did not show statistically significant differences in ventilatory mechanics. The HS group had lower PAP values during EVLP when compared to the SH group ($p = 0.013$). Treatment with in vivo hypertonic solution reduces the inflammatory levels of lungs undergoing hemorrhagic shock. Our study showed that the treatment with Saline Hypertonic Solution before EVLP stabilizes pulmonary artery pressure in ex vivo perfusion model in small animals.

BO97 AN ALGORITHMIC APPROACH FOR EARLY NON-INVASIVE AND RAPID DIAGNOSIS OF ACUTE LUNG ALLOGRAFT REJECTION UTILIZING NOVEL PCLE MARKERS WITHOUT LUNG BIOPSY

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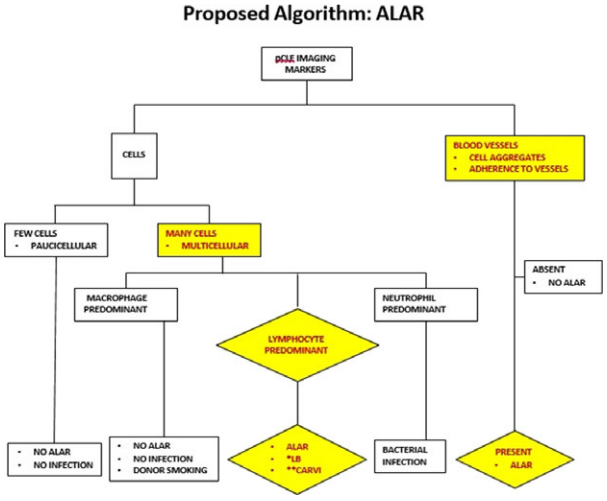
Background: Acute lung allograft rejection [ALAR] is a medical emergency. Early diagnosis and timely treatment is paramount to prevent graft loss. About 30–80% of all acute rejection episodes occur within the first 3–6 months following lung transplantation and, are clinically silent necessitating frequent transbronchial lung biopsy for detection. The procedure can be associated with significant complications and morbidity. We report our experience in utilizing probe-based confocal laser endomicroscopy (pCLE) markers [non-invasive] for the early diagnosis of ALAR without biopsy [invasive] and, propose an algorithm based on these markers.
Method: We performed pCLE in 30 patients; all were single or bilateral lung recipients within the first year after transplantation. All studies were performed per institutional guidelines under conscious sedation using a routine adult size flexible bronchoscope. Prior to performing a bronchoalveolar lavage (BAL) and transbronchial lung biopsies, the pCLE probe [Cellvizio©, Mauna Kea Technologies] was advanced through the working channel of the bronchoscope, under fluoroscopic guidance, to the visceral pleura and images were captured. pCLE markers that were presumed relevant were utilized for constructing the algorithm. Following pCLE, a bronchoalveolar lavage [BAL] for cell count and differential and transbronchial lung biopsies for pathology were performed and reviewed by a pathologist.

Findings and proposed algorithm:



*LB – Lymphocytic Bronchiolitis.
**CARVI – Community Acquired Respiratory Viral Illness.

Findings presumed to be prospective image markers to delineate ALAR and other processes:

Marker	Presumed process
Few cells	No infection/ALAR
Many cells	Infection or ALAR
Macrophage predominance	No infection/ALAR, possible smoking in donor
Neutrophil predominance	Bacterial infection
Lymphocyte predominance	ALAR, *LB, **CARVI
Vessels – cell adhesion/aggregates	ALAR
Normal vessels	No ALAR

*Lymphocytic Bronchiolitis
**Community Acquired Respiratory Viral Illness

Conclusion: pCLE markers seem promising, consistent and reproducible for the rapid assessment of alveolar cytology and blood vessel morphology. An algorithm utilizing these markers could potentially aid in the early, non-invasive and rapid diagnosis of ALAR and other active processes in the lung allograft without invasive lung biopsies and associated complications. We propose a pilot study to validate its utility.

BO98 TREATMENT OF ANTIBODY MEDIATED REJECTION AFTER LUNG TRANSPLANTATION: WHAT ARE WE DOING? PRELIMINARY RESULTS FROM A SINGLE CENTRE EXPERIENCE

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[1]Royal Brompton; [2]University Hospital of Cologne

Introduction: Pre-transplant human leukocyte antigen(HLA) donor-specific antibodies(DSA) are associated with poor graft survival after transplantation. De-novo DSA produced after lung transplantation(TX) has been shown to have an impact on development of Chronic-Lung-Allograft-Dysfunction(CLAD). There is no consensus for the diagnosis or treatment of AMR. We present our therapeutic approach for management of AMR
Methods: We stratified patients(from highly likely to unlikely)with suspected AMR according to a combination of clinical, histopathological and immunological factors. Only patients with highly likely or probable AMR were treated. Patients were also divided in early(EAMR) and late AMR(LAMR) according with time of onset of DSA from the TX. We defined EAMR when DSA were at least 6 weeks-but before 12 months from the TX. All patients with positive DSA after 12 months from TX were LAMR. The EAMR-group receive immunoabsorption, intravenous immunoglobulin and rituximab. The LAMR-group receive high dose steroids and rATG
Results: Four EAMR and four LAMR-patients were studied. All patients had negative donor cross-match. All EAMR patients had positive biopsies before treatment. This was negative in all after treatment. Improvement of LF was observed in all patients and conversion of DSA status was seen in two. The remaining two had a reduction of titre.In the LAMR-group, two patients had positive biopsies. This was negative in one patient after treatment; the other improved but remained positive. In the remaining two patients no histological features of AMR was observed. In two patients a conversion of DSA status was seen and the LF hasn't changed. One patient showed no improvement and was re-transplanted. One patient had a reduction in DSA titre but decline in LF was observed.
Conclusion: Early intervention for AMR seems to have positive effect in terms LF, biopsy featurof AMR and DSA.Further studies are needed to confirm our results and long-term follow up is warranted.

BO99* IMMUNOSUPPRESSIVE EFFECT OF AUTOLOGOUS ADIPOSE–TISSUE DERIVED MESENCHYMAL STEM CELL IN A RAT LUNG TRANSPLANTATION MODEL

Hironosuke Watanabe[1], Tomoshi Tsuchiya[1], Takuro Miyazaki[1], Keitaro Matsumoto[1], Naoya Yamasaki[1], Hiroshi Yukawa[2], Yoshinobu Baba[2], Takeshi Nagayasu[1]
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Purpose: Immunosuppressants are associated with various complications after lung transplantation, and thus less intense immunosuppression should be attempted. Adipose tissue-derived mesenchymal stem cells (ADMSCs) were recently found to have an immunomodulatory effect in various disease models through the secretion of hepatocyte growth factor (HGF).The purpose of this study was to investigate the effect of ADMSCs on immune response in a rat lung transplantation model.
Materials and Methods: Orthotopic left lung transplantation was performed by the cuff technique. Before transplantation, rats' own ADMSCs were gathered from the abdominal subcutaneous adipose tissue and cultured. The experimental subjects were divided into four groups as follows: control group (C group), no treatment after transplantation; ADMSC group (AD group), a single intravenous injection of ADMSCs (autologous 1.0 × 10*6) after transplantation; tacrolimus group (T group), administration of tacrolimus (0.5 mg/kg) every 24 h after transplantation; and ADMSC and tacrolimus group (AT group), a single intravenous injection of ADMSCs(autologous 1.0 × 10*6) after transplantation in combination with tacrolimus (0.5 mg/kg) every 24 h. Allografts were then assessed histologically and serum HGF levels measured.
Results: Although no significant differences were found between the C and AD groups, the histologic rejection grade of the AT group was significantly lower than that of the other groups. The bronchus-associated lymphoid tissue cell proliferating cell nuclear antigen index of the AT group was significantly lower than that of the T group. The serum HGF level of the AT group was significantly higher than that of the T group at postoperative days 3 and 7. The expression of cMet, the tyrosine kinase receptor of HGF, significantly increased in the AT group compared with that of the T group.
Conclusion: ADMSCs combined with tacrolimus reinforced immunosuppression, possibly due to the secretion of HGF.

BO100

EARLY NON-INVASIVE AND RAPID DIAGNOSIS OF ACUTE LUNG ALLOGRAFT REJECTION WITHOUT LUNG BIOPSY: IS PCLE A BREAK THROUGH THAT COULD CHANGE THE PRACTICE?

Ramachandra Sista, Karen Swanson, Cesar Keller
Mayo Clinic

Background: Acute lung allograft rejection [ALAR] is a medical emergency. Early diagnosis and timely treatment is paramount to prevent graft loss. About 30–80% of ALAR episodes occur within the first 3–6 months after transplant and, are clinically silent necessitating frequent transbronchial lung biopsy with its potential complications for detection. We report preliminary results of a novel probe-based confocal laser endomicroscopy [pCLE] procedure [non-invasive] for early and rapid diagnosis of ALAR without biopsy [invasive] and associated complications.

Method: We performed pCLE in 25 patients within the first year after single or bilateral lung transplant. Studies were performed per institutional guidelines under conscious sedation using a routine adult sized flexible bronchoscope. The pCLE probe [Cellvizio©, Mauna Kea Technologies] was advanced through the working channel of the bronchoscope, under fluoroscopic guidance, to the visceral pleura and images were captured. Findings presumed to be prospective markers to delineate ALAR and other processes are listed in the table below. A lung lavage with cell counts and transbronchial lung biopsies were performed for pathology review.

Findings:

Findings presumed to be prospective image markers to delineate ALAR and other processes:

Marker	Presumed process
Few cells	No infection/ALAR
Many cells	Infection or ALAR
Macrophage predominance	No infection/ALAR, possible smoking in donor
Neutrophil predominance	Bacterial infection
Lymphocyte predominance	ALAR, *LB, **CARVI
Vessels – cell adhesion/aggregates	ALAR
Normal vessels	No ALAR

*Lymphocytic Bronchiolitis
**Community Acquired Respiratory Viral Illness

*Lymphocytic Bronchiolitis.
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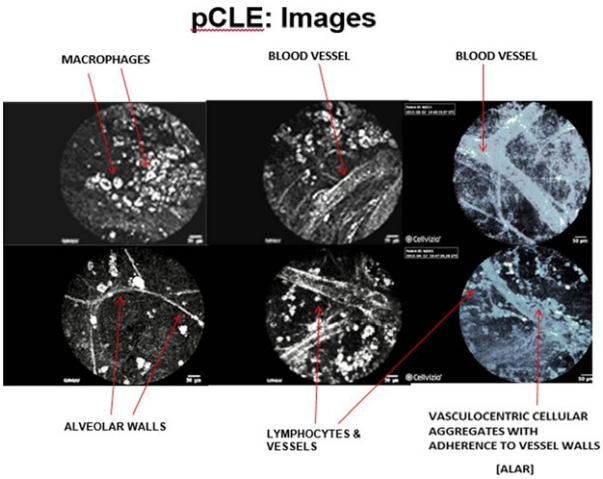


Conclusion: pCLE markers seem promising in the rapid, non-invasive diagnosis of ALAR and other active processes in the transplante.

023 KIDNEY

BO101 A SIMPLE AND SAFE METHOD IN ABO INCOMPATIBLE RENAL TRANSPLANTATION: MULTICENTER EXPERIENCES FROM CHINA

Yi Wang[1], Gang Chen[2], Tao Lin[3], Hongtao Liu[4], Jiqiu Wen[5], Changxi Wang[6], Zhigang Luo[1], Peigeng Gui[1], Hongtao Jiang[1], Hao Zhou[1], Guoqin Qin[1], Yizhou Zou[7]

[1]The Second Affiliated Hospital, University of South China; [2]Institute of Organ Transplantation, Tongji Hospital Huazhong University of Science and Technology; [3]Department of Urology /Organ Transplantation Center, West China Hospital, Sichuan University; [4]The Organ Transplantation center of Anhui Provincial Hospital; [5]National Clinical Research Center of Kidney Disease, Jinling Hospital Nanjing University School of Medicine; [6]Organ transplantation Center, the First Affiliated Hospital of Sun Yatsen University; [7]Department of Immunology,Xiangya Medical School,Central South University

Objectives: To introduce a simple, safe and effective method desensitization protocols in ABO-incompatible (ABOi) kidney transplantation, which has been used in multicenter in China.
Methods: 19 ABOi kidney transplantations (KTs) were performed between Sept.2010 and Dec. 2014 in 4 centers in China. We collected the perioperative and follow-up data for 19 of these patients until Dec. 2014. The preconditioning and immunosuppressive protocols were almost identical across the different transplant centers, with rituximab before 21 and tacrolimus-based immunosuppressants. Only one time DFPP and/or no one time plasmapheresis (PP) with the target of anti-A/B antibody titer 1: 8 or 1: 16 on the operation day.
Results: During the 51-month period of studies, the mean follow-up period was 22 months (range, 2–51 months), 19 kidney Patients survival was 100%, with allograft survival of 94.7%. For desensitization, 12 cases only 1 time DFPP and 1 time PP, 9 cases only one time DFPP and no any PP.Starting isoagglutinin IgG and IgM titers ranged from 1:4 to 1:1024 and 1:2 to 1:256 respectively. The mean starting IgG and IgM titers were 1:128 and 1:64 severally. The kidney transplantation was performed the day only if the post – DFPP and/or no PP IgM and IgG antibody titers were below 1:8. Mean (SD) creatinine levels, a measure of graft function, were 456.3 (33.5) μmol/l at discharge, 107.9(11.4) μmol/l at 1 month, 103.1(12.2) μmol/l at 3 months, 104.6 (9.3) μmol/l at 6 months, and 96.1 (10.9) μmol/l at 1 year. One accelerated acute rejection occurred (this case received stem cell treatment before kidney transplantation).
Conclusions: These results suggest that with this simple regimen of desensitization in ABO-incompatible (ABOi) kidney transplantation is possible and safe. Meanwhile, acceptable results and graft function are obtainable, In particular, the result increases the possibility of the application of deceased donors in the ABO-incompatible kidney transplantation.

BO102 TRANSPLANT ACROSS THE BLOOD GROUP BARRIER – A SINGLE CENTER EXPERIENCE FROM EASTERN INDIA

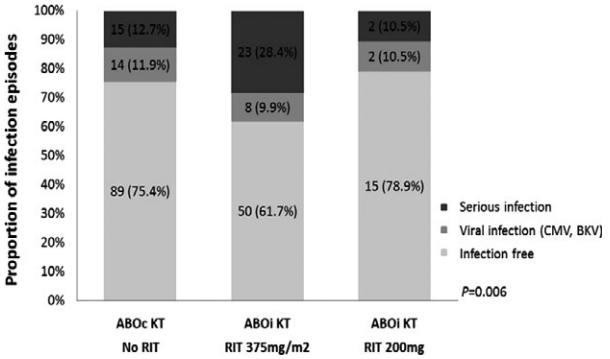
Sharmila Thukral, Deepak S. Ray
Narayan Health (RTIICS)

Background: With the incessantly increasing number of patients on wait list for renal transplant, expansion of donor pool is essential. In India, most of the renal transplants are living related. Almost 30% of otherwise suitable donors are rejected because of ABO incompatibility (ABOI), so removing the blood group barrier can increase donor pool substantially. We started ABOI renal transplantation 2013 with a relatively low cost de-sensitisation programme (additional cost~1200 dollars). This is a study of the short term outcomes of ABOI renal transplants.
Methods: Thirty patients who were ABOI were included in the study. All of them underwent a pre-transplant desensitisation programme, which included conventional plasmapheresis, IVIG and Rituximab. A pre-transplant antibody titer of ≤1:8 was considered acceptable for transplant following which Post transplant monitoring of antibody titers were done.
Results: Out of 30 renal transplant recipients 50% were of Blood Group O. The maximum initial antibody titre was 1:512. All patients achieved immediate graft function post-transplant. The mean serum creatinine at discharge was 1.21 mg% and mean ab titre at discharge was 1:4. One graft was lost due to severe AMR with cortical necrosis. 1- year graft survival was 96.6%. Mortality rate was 3.5% - one patient died with a functioning allograft due to sepsis secondary to Multi drug resistant Acinatobacter infection. The overall result in terms of graft and patient survival, infections and rejection were similar to ABO compatible transplants.
Conclusions: ABOI renal transplantation is a good modality to increase the donor pool especially in those parts of the world where deceased donor program is difficult to implement. Contrary to the belief that it is extremely expensive we have had good outcomes with a low cost protocol of desensitisation.

BO104* INFECTIOUS COMPLICATIONS IN ABO INCOMPATIBLE KIDNEY TRANSPLANTATION RECIPIENT ACCORDING TO THE RITUXIMAB DOSE

Juhan Lee, Jae Geun Lee, Seung Hwan Song, Shin Young Kim, Man Ki Ju, Dong Jin Joo, Myoung Soo Kim, Soon Il Kim, Yu Seun Kim, Hyun Ok Kim, Kyu Ha Huh
Yonsei University College of Medicine

Background: Desensitization with rituximab and intravenous immunoglobulin improves ABO incompatible (ABOi) kidney transplantation (KT) outcomes. However, infections have been noted in association with rituximab administration. In this study, we retrospectively compared infectious outcomes between ABOi KT and ABO compatible (ABOc) KT according to rituximab dose.
Methods: We analyzed 218 consecutive recipients (118 ABO compatible, 100 ABO incompatible) who underwent kidney transplantation from living donor between June 2010 and July 2014. ABOi KT patients were categorized by rituximab dose (375 mg/m^2 standard dose vs. 200 mg reduced dose). All patients received basiliximab for induction immunosuppression and maintained on triple immunosuppression consisting of tacrolimus, prednisone, and mycophenolate mofetil.
Results: During an average follow-up of 23 months, overall patient survival was 99 and 98%, and graft survival was 99 and 96% in the ABOc and ABOi groups, retrospectively. A total of 31 patients (38.3%) in the standard rituximab group in ABOi KT and 29 patients (24.6%) in the ABOc KT group diagnosed with infection ($p = 0.027$). There was one death in standard dose rituximab group related to infection (1%). Afterward, we reduced the dose of rituximab to 200 mg to decrease the infection risk in August 2013 ($n = 19$). Four patients (21.0%) diagnosed with infection in reduced dose group in ABOi KT. The rejection rate was not significantly different between rituximab groups in ABOi KT.
Conclusion: Standard dose of rituximab increase infection risk when used for desensitization. Reduced dose of rituximab might be sufficient for blood type incompatible desensitization without increase the risk of serious infections.



BO105 EFFECT OF DESENSITIZATION PROTOCOL CONSISTING OF TWO DOSES RITUXIMAB AND 4 WEEKS TREATMENT WITH MYCOPHENOLATE MOFETIL IN ABO-INCOMPATIBLE HIGH TITER KIDNEY TRANSPLANT RECIPIENTS

Shunji Nishide, Junji Uchida, Tomoaki Iwai, Kazuya Kabei, Nobuyuki Kuwabara, Toshihide Naganuma, Norihiko Kumada, Tatsuya Nakatani
Osaka City University Graduate School of Medicine

Background: ABO-incompatible high titer kidney transplantation is still considered to be high risk due to uncontrollable severe antibody-mediated rejections, and it has remained a medical challenge. Previously, we demonstrated a desensitization protocol for ABO-incompatible high titer kidney transplantation consisting of rituximab administration, splenectomy, and pharmacological immunosuppression. The purpose of this study was to assess the effect of two doses rituximab and 4 weeks treatment with mycophenolate mofetil (MMF) before transplantation.
Methods: We treated 8 patients with high (≥1:512) anti-A/B antibody titers. Our immunosuppressive regimen was initiated 1 month before surgery and included MMF administration. Two doses of rituximab were administered 2 weeks before and on the day of transplantation. We performed antibody removal with 6-10 sessions of plasmapheresis before transplantation. Splenectomy was performed at the time of transplantation in all patients. The B cell count in the peripheral blood was analyzed with a fluorescence-activated cell sorter using anti-CD19 and -CD20 antibodies, and B cells in the spleen were analyzed by immunohistochemistry using anti-CD 20 and -CD 79a antibodies.
Results: Of the eight patients, 7 subsequently underwent successful living-donor kidney transplantation. Although one patient received 8 sessions of

plasmapheresis, the antibody titer rebounded and remained ≥1:512. This patient underwent splenectomy only and continued to receive MMF 0.5 g/day. Among the patients receiving kidney transplantation, 3 patients experienced anti-A/B titer rebound less than four times after antibody removal and 4 patients experienced rebound more than 4 times. B cells were completely eliminated from the circulation for 3 months after transplantation in all patients. Immunohistochemical examination of the spleen showed complete elimination of B cells in the white pulps in the patients who experienced rebound less tha.

BO106 LONG-TERM RESULTS OF ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

Christina Melexopoulou[1], Smaragdi Marinaki[1], Chrysanthi Skalioti[1], Maria Darema[1], Giorgos Liapis[2], Giorgos Zavvos[3], John Boletis[1]

[1]Nephrology Department & Transplantation Unit, "Laiko" General Hospital; [2]Pathology Department, University of Athens; [3]Transplantation Unit, "Laiko" General Hospital

Background: Shortage of available transplant organs worldwide has implemented renal ABO-incompatible (ABOi) kidney transplantation (KTx) as a potential therapeutic strategy for end-stage renal disease (ESRD) patients. We report the long-term results of the unique center in Greece performing ABOi KTx.
Methods: From June 2005 to December 2013, 30 consecutive ABOi KTx were performed. We followed slightly modified the Swedish protocol. More specifically we used rituximab, the immunoadsorptions (IA) [preoperative target IgG ABO antibodies (ab) titer≤1:16], intravenous immunoglobulin, double oral immunosuppression (everolimus plus tacrolimus or tacrolimus plus mycophenolate acid) instituted 15 days pre-KTx and corticosteroids from the day of surgery. As a control group we randomly selected 30 ABO-compatible (ABOc) living KTx, a group with similar baseline characteristics to the ABOi KTx group.
Results: The mean follow-up period was 6 years(y) [range 1 to 9 y]. A mean of 5.1 ± 3.1 IA pre-KTx were required. Patient survival in ABOi KTx in comparison to ABOc KTx at 1, 5 and 8 y did not differ significantly (100% vs. 100%, 92% vs. 100% and 92% vs. 100%, p = ns). Additionally, graft survival was similar in the two groups (100% vs. 100%, 92% vs. 96% and 81% vs. 92%, p = ns). None of the patients developed acute antibody-mediated rejection. Four patients (13.3%) in ABOi group and 3 (10%) in ABOc group experienced acute cellular rejection, which was treated successfully. The mean serum creatinine at 1, 5 and 8y did not differ significantly between the two groups (1.56 ± 0.34 vs. 1.53 ± 0.46, 1.6 ± 0.5 vs. 1.53 ± 0.55 and 1.78 ± 0.57 vs. 1.76 ± 0.58 mg/dl, p = ns). Also, bacterial and viral infection episodes were similar between the two groups.
Conclusion: ABOi KTx is a safe and effective therapeutic strategy for the management of ESRD patients and potentially could contribute to the enlargement of the living donor pool.

BO107 RITUXIMAB IS MORE EFFECTIVE ON SUPPRESSION OF DE NOVO ANTI-DONOR BLOOD GROUP ANTIBODY THAN SPLENECTOMY AND ANTIBODY REMOVAL PROCEDURE IN ABO INCOMPATIBLE KIDNEY TRANSPLANTATION

Ken Sugiyama[1], Atsushi Aikawa[2], Yoji Hyodo[2], Takeshi Kawamura[2], Seiichiro Shishido[2], Ken Sakai[2]

[1]Departmento of Urology, Ota Memorial Hospital; [2]Department of Nephrology, Toho University

Aim: The aim of this retrospective study is to investigate whether immunosuppression including rituximab (RIT) is effective on suppression of anti-donor blood group antibody IgG (ADBGAb) in ABO incompatible kidney transplantation (ABOi).
Patient and Method: One hundred thirty four ABOi recipients were entered in this study. The recipients were divided into 3 groups in terms of immunosuppression (IS) protocols. IS consisted of azathioprine (AZA), steroid and cyclosporine (CsA) including splenectomy (Spx) in 62 recipients (AZA group). Basiliximab, mycophenolate mofetile (MMF), steroid and CsA or tacrolimus (FK) including Spx were given in 33 (MMF group). MMF, steroid and basiliximab, RIT and CsA or FK were given in 39 (RIT group). Ten recipients with low titer of ADBGAb (<64) in RIT group were not performed pre-transplant (Tx) antibody removal procedures (ARP). Post-Tx ARP were not performed. The titers of ADBGAb, the graft survival rates, incidence of biopsy proven antibody mediated rejection (AMR) were studied.
Results: The patients profile was not different in 3 groups. The titer of ADBGAB before pre-Tx ARP in AZA group (154 ± 241) was higher than RIT group (57 ± 98; p < 0.009), however not different between AZA and MMF (160 ± 387) groups, and between MMF and RIT groups. Maximum titer of post-Tx ADBGAB was significantly lower in RIT group (10 ± 15) than AZA (76 ± 137; p < 0.002) and MMF (54 ± 96; p < 0.004) groups. The graft survival rates were 89%, 100% and 95% at 1 year, 75%, 97% and 95% at 5 years, in AZA, MMF and RIT groups respectively. One recipient in AZA group had hyperacute rejection. Incidence of AMR was significantly lower in RIT group (8%), than AZA (32%; p < 0.05)) and MMF (18%; p < 0.05). 10 ABOi recipients without pre-Tx ARP had no clinical acute rejection including AMR.
Conclusion: The rise of the titer of post-Tx ADBGAb appeared to be due to *de novo* Ab. Therefore RIT appeared to be more effective on remaining low ADBGAb and better outcomes than Spx and ARP.

BO108 LONG TERM ABO ANTIBODY TITRE MEASUREMENTS AFTER ABO-INCOMPATIBLE TRANSPLANTATION

Rasneet Nagi[1], Miriam Manook[2], Lionel Couzi[3], Nicos Kessaris[2], Anthony Dorling[2], Nizam Mamode[2]

[1]KCL; [2]Guy's & St Thomas's Hospital; [3]Centre Hospitalier Universitaire de Bordeaux

Introduction: Long-term outcomes of ABO incompatible kidney transplantation (ABOi-KT) are comparable to those of compatible transplantation with respect to patient survival, graft survival and graft function. However, little is reported regarding ABO antibody (Ab) measurements after the initial post-transplant period. We wanted to assess outcomes >5 years post ABOi-KT to see whether early post-transplant rise influenced long term graft survival and function.
Methods: In a single centre, 37 patients had an ABOi-KT performed >5 years ago (transplanted 2005-2009) and received pre-transplant antibody desensitisation according to baseline titre. Graft survival, patient survival, creatinine and eGFR levels were recorded annually and post-transplant Ab titres were recorded on a linear scale (no. of dilutions). Patients were grouped according to their 1 month post-transplant Ab measurement; those with an Ab RISE, (i.e. a > 2 dilution increase in Ab from pre-transplant) versus NO RISE.
Results: In the cohort, 5 patients were lost to follow up, graft and patient survival for the remaining 32 at a mean follow up time of 78 months were 93.8% and 90.6% respectively. Mean Ab dilution was measured at baseline (6.81 ± 2.31), pre transplant (3.46 ± 1.04), 1 month (3.00 ± 1.97), 1 year (2.58 ± 1.91) and >5 years (2.44 ± 2.09). At >5 years, a significant decrease in ABO Ab was found from baseline (p = 0.20), 1 month (p = 0.72) or 1 year (p = 0.69). 9% of the cohort had an early Ab RISE, 1 patient received post-operative Ab removal. In the NO RISE group, between 1 m - > 5 years, 11 had a fall in Ab levels, 3 had no change and 2 had an increase. Comparing the RISE versus NO RISE groups, graft survival, patient survival and graft function were not significantly different.

Discussion: Early ABO Ab rise appears to have no effect on long-term graft or patient outcomes >5 years post ABOi-KT. Similarly, long-term ABO Ab levels are variable and do not reflect clinical outcomes.

BO109 HIGH- VERSUS LOW-TITER ANTI-ABO ANTIBODY IN ABO INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION

Jin Kong[1], Byung Kim[2], Joon Jeong[2]

[1]Hanseo Hospital; [2]Maryknoll Hospital

ABOi KT is now an established procedure with outcomes equivalent to ABO compatible KT. The impact of pretransplant high anti-ABO antibody on the outcomes of ABOi KT is not well established. Among 75 ABOi KT patients, initial anti-ABO titer was ≥128 in 47 patients (high-titer group) and ≤64 in 28 patients (low-titer group). Rituximab was routinely administered. No patient underwent splenectomy. Pretransplant plasmapheresis aimed anti-ABO titer at ≤8 on transplant day, but those patients whose antibody could not be lowered to the target by transplant day were also underwent transplantation. Posttransplant preemptive plasmapheresis during 2 weeks was not performed routinely but as needed in patients with higher antibody titer or increase in creatinine while awaiting biopsy result. Median (range) anti-ABO titer at initial, on transplant day and at 2 weeks was 256 (128–4096), 8 (2–16), and 8 (1–32), respectively, in high-titer group. 32 (8–64), 2 (1–4) and 2 (1–4), respectively, in low-titer group. Biopsy-proven acute rejection (BPAR) occurred in 5 patients in high-titer group, and in 5 in low-titer group. Among these 10 BPAR, 4 were antibody mediated rejection (AMR), 3 in high-titer and 1 in low-titer group. Two cases of AMR seems to be induced by anti-HLA antibody since donor specific anti-HLA antibody (DSA) was detectable by Luminex SAB during AMR, and anti-ABO titer was low (≤4) during AMR. The other 2 cases of AMR was attributable to anti-ABO antibody since no DSA was detectable and anti-ABO antibody was high(16) during AMR. All the BPAR were recovered by treatment.
Conclusion: High anti-ABO antibody titer before transplantation dose not impact outcomes of ABOi KT. Clinical AMR (AMR with graft dysfunction) is rare under current preconditioning and immunosuppressive protocol. DSA seems to play a major role in the development of AMR in ABOi KT.

BO110

RISK FACTORS OF POSTOPERATIVE BLEEDING IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION

Mi-Hyeong Kim[1], Kang-Woong Jun[1], Sang-Hyun Ahn[2], Sang-Dong Kim[3], Sun-Cheol Park[4], Sang-Il Kim[1], In-Sung Moon[1], Ji-Il Kim[1]

[1]Seoul St. Mary's hospital The Catholic University of Korea; [2]Yeouido St. Mary's hospital, The Catholic University of Korea; [3]Incheon St. Mary's hospital, The Catholic University of Korea; [4]Uijungbu St. Mary's hospital, The Catholic University of Korea

Introduction: The outcome of ABO-incompatible kidney transplantation (ABOi KT) has improved to be comparable to that of ABO-compatible kidney transplantation by the advancement of the antibody depletion technique and immunosuppressants. However, a lot of researchers reported a high risk of bleeding after ABOi KT. This study aimed to analyze the risk factors of bleeding in patients with ABOi KT.

Methods: Seventy patients with ABOi KT were retrospectively analyzed. A bleeding incident occurred in 9 patients. We examined general characteristics, immunologic characteristics, hematologic characteristics and an immediate graft loss.

Results: The preemptive transplantation before initiating dialysis respectively an elevated pre-transplant blood urea nitrogen were significantly common in recipients of ABOi KT ($p = 0.0176, 0.023$). On univariable analysis, a high anti-ABO antibody titer after plasmapheresis ($\geq$ 1:16), a drop of platelet count $\leq$100 000/mm^3 after plasmapheresis ($p = 0.0226$), a prolonged activated partial thromboplastin time ($p = 0.0289$) and an impairment of platelet function ($p = 0.0073$) were significantly associated with the increment of bleeding risk after ABOi KT ($p = 0.0274$). However, on multivariable logistic regression analysis, only preemptive transplantation was significantly related to the increase of bleeding risk after ABOi KT ($p = 0.0239$). The occurrence of immediate graft loss was significantly high in patients with bleeding incident ($p = 0.015$).

Conclusion: Bleeding after ABOi KT is a very serious complication. It is difficult to control and increases the risk of immediate graft loss. We have to recognize the risk factors and adjust the correctable factors before and after transplantation and to concentrate on a meticulous hemostasis during surgery.

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025 LIVER

BO111 LIVER TRANSPLANTATION IN FAMILIAL HYPERCHOLESTROLEMIA

Mohsen Reza Mansoorian[1], Kourosh Kazemi[1], Saman Nikeghbalian[1], Alireza Shamsaeefar[1], Maral Mokhtari[2], Seyed Mohsen Dehghani[3], Ali Bahador[1], Heshmatollah Salahi[1], Hamid Amoozgar[4], Siavash Gholami[1], Goli Mehrdad[1], Seyed Ali Malek Hosseini[1]

[1]Organ transplant department Shiraz University of medical sceinecs; [2]Pathology department, Shiraz University of Medical Sciences; [3]Pediatric Gastroenterology and Hepatology, Shiraz University of Medical Sciences; [4]Cardiac and neonatology research center, Shiraz University of Medical Sciences

Background: Familial hypercholesterolemia (FH) is an autosomal genetic disorder caused by different mutation in low-density lipoprotein (LDL) receptor gene. The afflicted patients are at increased risk of premature atherosclerosis and myocardial infarction. Liver transplantation is introduced as a treatment option in medical-therapy refractive cases.
Material and Method: A retrospective review of transplant center database of Namazi hospital, affiliated to Shiraz University of Medical Sciences, Shiraz, Iran during between 2008–2014 revealed about 1880 liver transplantation cases. Among them, 36 patients were transplanted due to FH. All the patients were diagnosed based on clinical findings and cholesterol values.
Result: Of 36 FH patients, 20 were male and 16 were female with an age range of 2.5 to 28 years. The most common clinical sign of the patients were cutaneous Xanthoma followed by Arcus senilis.18 patients had premature coronary artery disease. 11 patients underwent coronary artery bypass graft and 7 patients were treated by percutaneous coronary stenting. The majority of patients had LDL-C value of more than 500 mg/dl. 28 patients received orthotropic deceased donation whole liver transplantation. Five patients underwent living donor liver transplantation and 3 patients received split deceased donation liver transplant. Surgical and medical complications after liver transplantation was as follows: biliary stricture in two patients treated by Roux en Y procedure. Internal bleeding, septicemia, cytomegalovirus colitis, convulsion and liver abscess each in one patient and five patients showed mild acute rejection. One and 5-years-survial of the patients were 94% and 91%, respectively and graft survival was 97% and mortality was 8% (due to cardiac arrest and septicemia).
Conclusion: Liver transplantation should be considered in FH patients unresponsive to medical therapy ideally prior to the occurrence of significant cardiovascular disease.

BO112 DOMINO TRANSPLANTATION USING MSUD LIVERS: TECHNIQUE AND LONG TERM OUTCOMES

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Aim/Background: Domino liver transplantation (DomLT) using allografts with metabolic disorders enhances organ utilization but is not well described in children. Documentation of short and long term outcomes of these patients is critical to decision making about the safety of this procedure; we reviewed the outcomes of DomLT patients and their Maple Syrup Urine Disese (MSUD) donors at a single center.
Methods: All primary MSUD recipients and their paired donors receiving DomLT were analyzed retrospectively with minimum 1 year follow-up period for patient and donor characteristics, postoperative complications and patient and graft survivals. Age, weight, cold ischemia time, postoperative leucine levels and peak ALT (alanine aminotransferase) levels during postoperative 48 h were compared among these pairs.
Results: Between 2007 and 2014, 9 patients underwent DomLT receiving live-donor allografts from MSUD patients. The indications were progressive familial intrahepatic cholestasis ($n = 1$), cystic fibrosis ($n = 1$), congenital hepatic fibrosis ($n = 2$), embryonal sarcoma ($n = 1$), primary sclerosing cholangitis ($n = 2$), chronic rejection after liver transplantation ($n = 2$). Technical modifications utilized included hepatic vein venoplasty in one patient. There was no vascular complication in early postoperative period; one patient who required SMV graft at time of domino transplant had graft thrombosis 3 year after transplantation and underwent successful Meso-Rex shunt.

The data and comparison between DomLT and MSUD recipients were listed in the Table below:

Recipient demographics and functional metrics	MSUD recipient	DomLT recipient	p-Value
Mean age at transplantation (years)	15.87	23.96	0.06
Mean weight (kg)	49.32	59.71	0.12
Posttransplant mean leucine level (umol/dL)	18.11	12.33	0.05
Posttransplant mean cold ischemia time (minute)	370.33	303.88	0.20
Posttransplant peak ALT in 48 h (IU/l)	1047	303	0.002

Conclusion: Patient and graft survival in DomLT from MSUD donors has been excellent at long term follow-up. Metabolic function has been normal in all recipients on normal unrestricted protein intake. Ischemia preservation injury based on peak ALT has been significantly decreased in DomLT recipients. Domino transplant from pediatric and adult recipients with selected metabolic disease should be increasingly considered.

BO113 LIVER TRANSPLANTATION IN ADULTS AND CHILDREN WITH ABERNETHY MALFORMATION

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Background: Congenital absence of portal vein with extra hepatic portocaval shunt [Abernethy malformation (AM)] is a rare anomaly of the splanchnic venous system. In 70% of cases it is diagnosed in paediatric age, but may remain unknown until adulthood, up to 61 years. AM it is classified in types IA and IB with a complete portocaval shunt and type II with a partial side-to-side shunt and may be associated with pulmonary hypertension, hepatopulmonary syndrome, liver tumors and cirrhosis, thus requiring liver transplantation (LT).
Methods: We analysed the outcome of 2 adults and 3 paediatric patients with AM who LT. Both adults and 1 child received a full liver graft; 2 children received a split liver (segment II-III). All the donors were brain dead and the livers were splitted in situ.
Results: Four patients had type IB AM and 1 type II. Median age at LT was 11 years (range 1–42). Indications for LT in adults were 1 bleeding adenoma and 1 HCC while in paediatric patients were 1 hepatoblastoma and 2 porto-pulmonary syndrome. The median donor age was 30 years (range 12–72). Total ischemia time was 420 min (range 285–535). Portal vein reconstruction in both split liver recipients required an interposition donor vein graft. The only surgical complication was a biliary leak in one child receiving a split liver who 1 year later developed a portal vein thrombosis without manifestations of portal hypertension. Recover of pulmonary hypertension in 6 months. All patients are alive with normal graft function after a median follow up of 5 years (range 1–9). No recipient experienced tumor recurrence or relapse of the clinical manifestations.
Conclusion: Our results confirm the successful feasibility of LT for different manifestations of AM with low morbidity and optimal long-term survival. Portal vein reconstruction may be problematic and requires careful planning in these patients, especially when split grafts are used.

BO114 LIVER TRANSPLANTATION IN PATIENTS >65 YEARS – ANALYSIS OF LONG-TERM CLINICAL OUTCOME

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Background: Liver transplantation (LT) in patients >65 years is controversially discussed. In Europe, the number of elderly patients waiting for LT is increasing. Donor shortage requests a careful selection of possible organ recipients and therefore accepting elderly patients for transplantation is an important issue. We performed a single-center analysis of long-term outcome from patients receiving LT at the age of 66 or older.
Methods: Between 1996 and 2014, 111 patients >65 years old were listed for LT. 67 patients were transplanted, 23 died while on the waiting list and 18 were removed from the list (tumor progression $n = 7$, poor condition $n = 3$, clinical improvement $n = 8$). From the 67 transplanted patients, the median follow-up was 31.8 months (range, 0–193 months) and the mean MELD-off was 17.5 ($\pm$ 1.4).
Results: The indications for transplantation were tumor $n = 22$, viral $n = 14$, alcoholic $n = 12$, biliary disease $n = 7$, autoimmune $n = 3$, acute hepatic failure $n = 2$ and other cirrhosis $n = 7$. Patient overall 1y, 3y and 5y-survival rates were 71%, 58% and 48%, respectively. Transplanted patients with an age of 18–60 years showed a significantly better survival (log-rank 0.011) compared to those >65 years. However, there was no significant difference between patients of 61 to 65-years and patients >65 years (log-rank 0.683). In total, 40

patients died during the observation period. Reasons for death were infection $n = 13$, tumor $n = 13$ (*de novo* $n = 7$, recurrence $n = 6$), graft related $n = 4$, viral recurrence $n = 2$, cerebrovascular $n = 3$ and other $n = 3$.
Conclusion: Our analysis shows that LT in patients >65 years is associated with an acceptable long-term outcome. The reason for the relatively high percentage of elderly patients dying of tumor recurrence/*de novo* tumors and infections postLT might be an immunosuppressive side effect that is under-reported in classic age-limited drug studies so far. Re-evaluation and adaption of postLT patient management might further improve long-term outcome.

BO115 NONALCOHOLIC STEATOHEPATITIS AS INDICATION FOR LIVER TRANSPLANTATION IN EUROPE: DO WE CHOOSE THE RIGHT ORGANS FOR THE RIGHT RECIPIENTS?

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Background: Over the past years, nonalcoholic steatohepatitis (NASH) has emerged to become the third leading cause for liver transplantation (LT) in the US. Since 2002, chronic liver failure due to NASH has increased constantly.
Aim: The aim of this study was to investigate all adult patients with NASH, who underwent LT in Europe between 2002 and 2012.
Methods: We analyzed the European dataset of over 37.000 adult liver transplant recipients in collaboration with the European Liver Transplant Register (Paris – France), including the years 2002 until 2012.
Results: From 2002 to 2012, 37.612 adult patients underwent orthotopic LT in Europe. The male percentage accounted for 73.7% (27727/37612), female patients were only 26.1% (9855/37612; in <0.1% no sex was documented). The most common indication for LT was alcoholic cirrhosis with 39.8% (14956/37612), the incidence of NASH was documented with 0.9% (337/37612). The NASH group did not show any significant difference in overall patient survival when compared to other indications ($p = 0.681$; see Figure 1). Recipient BMI >40 did not impact on the outcome in the NASH patient group, but was a significant risk factor in the nonNASH cohort. Donor steatosis stratified as steatosis to mild, moderate and severe did not impact the outcome in the NASH group, whereas in the nonNASH patient cohort, the difference was significant ($p = 0.011$, see Figure 2).
Conclusion: Patients, who underwent LT due to NASH, did not have decreased survival rates when compared to other indications. Severe donor steatosis seems to have no influence on the survival outcome within the NASH group. Should we consider providing NASH patients with donor grafts regardless to their steatosis level that might diminish the gap between needed organs and their demand?

Figure 1:

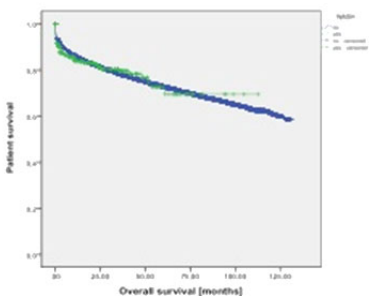
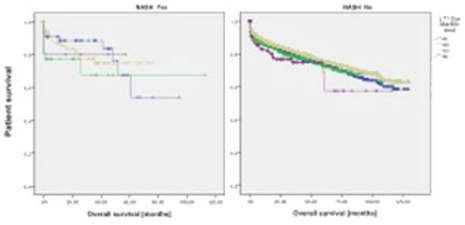


Figure 2:



BO116* LIVER TRANSPLANTATION FOR ALCOHOLIC LIVER CIRRHOSIS – LONG-TERM FOLLOW-UP IN RESPECT OF CLINICAL OUTCOME AND ALCOHOL RELAPSE

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Background: Liver transplantation (LT) for end-stage alcoholic liver disease (ALD) is although the second most common indication in Europe still discussed controversially. Especially, evaluation of alcohol abstinence prior to listing and long-term observation of a potential alcohol relapse is challenging. Biomarkers such as carbohydrate-deficient transferrin (CDT) might be used to identify alcohol relapse. We analysed outcome of patients with LT for ALD at the Medical University of Vienna.
Methods: Data from patients transplanted between 1996 and 2012 for ALD as main or secondary indication were included. A defined period of sobriety before listing was not obligatory. A specialist psychologist evaluated a possible alcohol relapse that was strictly defined as any post-LT alcohol consumption. CDT-levels were regularly measured postLT. Long-term patient and graft survival and incidence of alcohol relapse was evaluated.
Results: 382 patients with LT for ALD as primary ($n = 290$) or secondary ($n = 92$) indication reached a median follow-up of 73 months (0–213). 1y and 5y patient and graft survival was 82%, 69% and 82% and 75%, respectively. Total alcohol relapse rate was 16% with 4.8% and 12.9% at 1- and 3-years. Patients with ALD as main indication experienced significantly more often alcohol relapse (log rank; $p = 0.037$). Regularly post-LT measured CDT-levels showed a sensitivity of 94% and a specificity of 87%. In patients who died with alcohol relapse (32/186), death was significantly more often liver-related than in patients without alcohol relapse (154/186) (Chi-squared test; $p < 0.0001$).
Conclusion: This large single centre analysis describes excellent long-term outcome in LT for ALD. The alcohol relapse rate was low, although a defined abstinence period prior to listing was not applied and postLT alcohol relapse was defined strictly. CDT-levels measured postLT proofed to have high sensitivity and are therefore helpful tools to diagnose a potential alcohol relapse.

BO117 LIVER TRANSPLANTATION IN FAMILIAL AMYLOIDOTIC POLYNEUROPATHY: A 20 YEARS FOLLOW-UP STUDY

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Background and Aims: Familial amyloidoitic polyneuropathy (FAP) is an inherited, fatal, systemic disease where liver transplantation (LT) is an accepted treatment. Our aim was to characterize and evaluate the outcome of FAP patients undergoing LT.
Methods: Data from all FAP patients transplanted between 1992 and 2012 in one Portuguese LT centre were analyzed for demographics, FAP-related co-morbidities, disease duration previous to LT and cause of death. Long term survival was done using Kaplan–Meier survival curves. Logistic regression was used for multivariate analysis of survival predictive factors.
Results: During the study period, 361patients were transplanted for FAP, representing 25.8% of all LTs in the same centre. Median age at LT was 35 (range 21–67 years), with 186 males (51.5%). Prior to LT, median disease duration was 3 years (range 0–8 years). Forty two (11.6%) patients had to be re-transplanted. There were 45 deaths. Main causes of death were multiple organ failure (MOF) (18.8%), followed by sepsis (16.3%), vascular complications (7.7%), bleeding (4.7%), and stroke (4%). Overall survival at 1, 3, 5 and 10 years was 93.8%, 90.3%, 89.2% and 85%. Mortality predictive factors included in the model were age, disease duration, gender, presence of dysautonomia and neuropathy. Only age (6.7% increase for each year, $p = 0.002$) and disease duration previous to LT (20.8% increase for each year, $p = 0.016$) were significant. Almost 15% of FAP patients were transplanted more than 15 years ago, in the sub-group mean survival after the first symptoms was 18.2 years, comparing favourably with the mean survival time of 9–13 years, in the pre-transplantation era.
Conclusions: LT in FAP patients seems to be effective, associated with a very good long-term outcome, strongly suggesting an increase in survival. The main significant factors associated with mortality were disease duration prior to LT and age, thus suggesting the need for the procedure early in the course of disease.

BO118 PATIENTS WITH NON-V30MET TRANSTHYRETIN MUTATIONS: DATA FROM THE FAP WORLD TRANSPLANT REGISTRY (FAPWTR) SHOW LARGE VARIATION IN OUTCOME FOLLOWING LIVER OR LIVER/HEART TRANSPLANTATION

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Background: Hereditary transthyretin amyloidosis (ATTR) has been treated by liver transplantation (LTx) for over two decades. Different centres have reported the outcome of fairly large series of LTx ATTR Val30M patients, but for other mutations only few reports comprising small number of patients have been presented. We present the outcome after transplantation of non-ATTR Val30Met amyloid patients based on data reported to the FAP world transplant registry (FAPWTR).
Methods: Outcome data for all non-ATTR Val30Met patients registered in the FAPWTR was studied. The Kaplan-Meier method and log-rank test was used to analyse survival rates.
Results: The registry holds a total of 264 patients (males 174, females 90) with non-ATTR Val30Met mutations, representing 57 different mutations. The 9 most common mutations showed a considerable 10-year survival variation, ranging from 23% for Ser50Arg to 85% for Val71Ala. All mutations, except the Tyr114Cys mutation, with leptomeningeal complications revealed poor survival.
Conclusions: The FAPWTR data revealed large survival variations not only between different mutations, but also between mutations with similar phenotypes. Some mutations, such as Leu111Met, Val71Ala and Leu58His showed excellent survival. We want to stress that patients with other mutations than Val30Met are not a homogenous group, and we propose the term "non-Val30Met" to be used with caution and best be avoided. For several mutations data is still too limited to evaluate the efficacy of LTx, and it is therefore vitally important with continuous international collaboration to obtain more knowledge and further improve treatment guidance.

BO119 RESULTS OF LIVER TRANSPLANTATION IN THE TREATMENT OF HEPATIC ALVEOLAR ECHINOCOCCOSIS

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Background: Alveolar echinococcosis (AE) is a rare disease caused by the Echinococcus multilocularis larvae growing in the liver. This observation suggests that liver transplantation (LTx) may be indicated when other therapies become ineffective and no extrahepatic lesions are founded. The purpose of this study was to assess the value and timing of LTx in the treatment of AE of the liver.
Material and Methods: A retrospective study was carried out, including all cases of LTx for AE performed in our Department between 2000 and 2014. There were 23 cases AE (17M, 6F) in middle age of 43 ± 13. In 18 cases (78%) LTx was a priori decided to be the method of management due to the advancement of the disease preventing radical surgery. In 5 cases (22%) prior surgery led to the LTx (one extensive liver resection, one unresectable alveococcosis recurrency within the liver and two cases of diagnostic laparoscopy/laparotomy). 11 classical and 12 piggy-back LTx from cadaveric donor were performed. All of the patients received additionally albendazol, prior to and after LTx – mean period 2 years.
Results: Complications were observed in 6 cases (26%) – wound infection in 4 cases, pneumonia in 1 and in 1 transient renal filure requiring dialysotherapy. Two patients (10%) died within the 1st post-LTx year – 1 due to sepsis leading to multiorgan failure. 2nd patient died 7 months after LTx due to sepsis after small bowel resection in the course of mechanical occlusion. In group of 6 patients appeared immunological exponents of infection recurrence in ELISA test, without changes in imaging examinations, after average 24 ± 12 months. Actuarial survival rate after LTx was 91% at 1 year, 85% at 5, and 75% at 10 year.
Conclusion: Echinococcosis multilocularis of the liver in late stage can be considered as one of the indications of LTx, especially when other therapies are scarce and ineffective. In those cases LTx may be an appropriate option of radical treatment with excellent long term survival.

BO120 LIVER TRANSPLANTATION FOR NONALCOHOLIC STEATOHEPATITIS: ORGAN WASTE OR SUCCESSFUL TREATMENT OF THE NEW EPIDEMIC? A SINGLE CENTER EXPERIENCE

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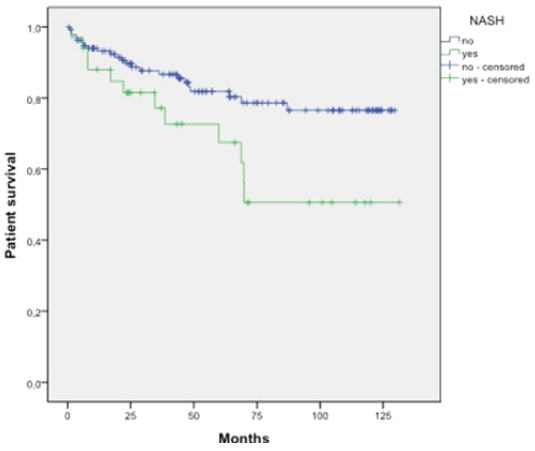
[1]Innsbruck Medical University; [2]Charite Berlin

Background: Nonalcoholic steatohepatitis (NASH) may become one of the leading indications for liver transplantation (LT). The aim of this study was to describe the clinical outcome.
Methods: This is a retrospective analysis of 515 patients who underwent LT between 2002 and 2012.
Results: The incidence of NASH as primary indication for LT was 14.4% (74/515). The study population included 116 (22.5%) women and 399 (77.5%) men. NASH cohort compared to the nonNASH cohort showed no significance on patient survival ($p = 0.109$). Patients with a malignancy displayed a shorter overall survival ($p = 0.009$). Average MELD score was 21.0, average BMI 25.3. Patients with a lower MELD score at time of LT were associated with a significantly better overall survival ($p = 0.043$). BMI >30 kg/m^2 had no impact on survival, neither in the NASH nor in the nonNASH cohort. Diabetes was diagnosed in 124 patients, compared to the patient cohort with no evidence of diabetes, overall survival was significantly shorter ($p = 0.006$). NASH patients with diabetes had similar overall survival and complications when compared to NASH patients without diabetes ($p = 0.242$; $p = 0.112$ respectively). Donor data such as donor BMI >30 kg/m^2, sever steatosis, age >55 years, gender mismatch and cold ischemic time >14 h had no impact on patient survival. Infection rate was significantly higher in the NASH cohort compared to other indications ($p = 0.04$). NASH patients with HCC were associated with a significantly shorter overall survival compared to HCC patients with no evidence of NASH ($p = 0.02$) while graft survival was comparable in both cohorts (Fig. 1).
Conclusion: Metabolic comorbidities significantly impact on patient survival. NASH predicts an inferior outcome in patients with HCC compared to other liver diseases. Accurate preoperative treatment of metabolic disorders and intensified infection prophylaxis should be considered in patients undergoing LT. Criteria for patients with HCC and NASH should be revisited.

Figure 1:



007 DONATION/RETRIEVAL

BO121 SPECTACULAR SHORTENING OF THE KIDNEY WAITING LIST IN THE NETHERLANDS

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[1]Dutch Transplant Foundation; [2]Erasmus Medical Center

Background: One of the key challenges in transplantation is to adequately help the increasing number of patients on the waiting list. In the Netherlands (NL) an important source of organs for transplantation is deceased donation (DD), both donation after brain death (DBD) and after circulatory death (DCD). For kidney transplantation, however, there is the additional option of living donation (LD). In the NL the LD programme includes specified donation including directed (both related and unrelated), indirect (incl. cross-over), and unspecified donation.
Methods: Kidney donation, transplantation and waiting list data over the period 2000-2014 were collected in the national database at the Dutch Transplant Foundation.
Results: The mean number of deceased kidney donors remained stable with 206 per year in 2000–2011, but increased to 244 per year in the period 2012-2014. A significant 'structural' increase of DCDs was observed from 20.5% in 2000 to 47.2% in 2014. In the same period the number of (LD) transplants tripled from 173 in 2000 to 534 in 2014 including 21.4% and 54.7% non related, respectively.The total number of kidney transplants increased from 560 (with 31% LD) in 2000 to 1004 (with 53% LD) in 2014 resulting in a transplant rate of 63/mill inhabitants. The inflow on the kidney waiting list, however, increased from 649 in 2000 to 1212 in 2014. Due to increased living and deceased kidney donor activity, this resulted in a 51% decrease of the active kidney waiting list from 1277 in 2000 to 622 in 2014 and a decrease in the median waiting time of 1.3 years.
Conclusion: The combined efforts to increase the number of deceased donors and expand the LD kidney programme have reduced the active kidney waiting list considerably. This justifies that both deceased and life kidney donation should be encouraged.

BO122 DECEASED ORGAN DONATION AND TRANSPLANTATION ACTIVITY IN THE KINGDOM OF SAUDI ARABIA A 20 YEAR PERSPECTIVE: 1995–2004 VERSUS 2005–2014

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Objective: Organ transplantation is the best existing method for the treatment of end-stage organ failure. 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 adapting the critical pathways of organ donation from possible to potential to eligible to consent and to actual deceased donors (DD) in the kingdom.
Methods: A retrospective study comparing the nationwide figures and composition of the Critical Pathway of DD cases for 20 years from 1995 to 2004 compared with 2005–2014 of the Saudi Center for Organ Transplantation (SCOT).
Results: The study showed a remarkable increase in the total number of possible DD cases from 3689 of 1995-2004 to 5542 (+34%) of 2005–2014. The mean possible case per year in relation to the number of population for the first half of the 20 year period is 12.3 pmp as compared to 18.4 pmp on the latter. The rate of conversion from possible to potential is 59% (2278 and 3282 respectively). Moreover, eligible donors ascend its number from 1999 to 2641 (+30.5%) of which 542 (27% with 1.06 pmp) and 952 (36% with 1.58 pmp) respectively were consented for organ donation. The actual DD for the year 1995–2004 was 493 and 839 (+41%) for the year 2005-2014. In relation to the actual DD cases, there was a significant increase of 47.6% in the number of organs transplanted, from 1106 to 2113 and in addition, there was an increase of 26.7% (613 and 837 respectively) with the tissues recovered alongside during the retrieval of DD cases.
Conclusion: There is a notable increase in the number of possible DD reported and consented in the second half of the decade. There was also a significant increase in the actual DD. In relation to this, the various strategies being implemented to promote organ donation in every region of the kingdom are relatively effective in applying the critical pathways of deceased organ donation.

BO123 EXTENDING SUCCESSFUL RESULTS OF NPOM (NEW PERSIAN OPU MODEL) TO ALL UNIVERSITIES OF IRAN

Katayoun Najafizadeh[1], Tayebeh Piriaie[2], Keyhan Hadisadegh[2], Maryam Moftakhari[2], Shadi Shafaghi[1], Mohammad Jamali[2], Saba Tabatabaie[2], Mahdieh Hazrati[2], Ali Moshari[2], Sayed Ghasem Hashemian[2], Ebrahim Kazemi[2], Aval Zahra Ansari[3], Maryam Sajedi[2], Omid Ghobadi[4]
[1]Ministry of health and Medical Education; [2]Iran Medical University; [3]Lung Transplant Research Center, NRITLD; [4]Iranain Ministry of Health and Medical Education

Background: Inspite of 5000–8000 brain dead annually, the rate of organ donation was 6.7 PMP in 2011 in Iran. NPOM was designed in one of the Universities of Tehran in 2011 and could increase the rate of donation in this University area to 32.4 PMP.With successful results of the project in this OPU it was completed and extended to all Universities of Iran.
Method: NPOM is composed of: PPDDP(Persian Possible Donor Detection Project) TDDP(Telephone Donor Detection Program) PIP(Persian Inspector Project) HR(Hospital Reporting) PIEP(Persian Interviewers Education Program) PDMP(Persian Donor Maintenance Project) and many other parts With performing this project, rate of brain dead potential donor detection increased 7 times, organ donation increased to 32.4 PMP and family consent rate increased to 96.4%.With moving the designers of the NPOM to Ministry of health as Director and Deputy director of Organ donation and Transplantation, IrNOPT (Iranian Network for Organ Procurement and Transplantation) project was written included NPOM for all Universities. IrNOPT project was started in October 2014.The directors of OPUs and Chief coordinators from all Universities were trained during two courses (first one for teaching NPOM and the second one by TPM). Then all Universities were inspected for their activity about Organ donation and transplantation.
Results: Although it is only 4 months past from starting the IrNOPT project the number of OPUs increased from 16 to 53. The rate of organ donation increased significantly in 20 Universities.Rate of family consent increased from 37% to 70%.A couple of Universities started renal transplant up to now and the others are making that possible.
Conclusion: IrNOPT and specially NPOM are operable and repeatable projects that can make the same effects wherever they use. These projects might be helpful for other countries and could make a big difference there.

BO124 CZECH NATIONAL KIDNEY EXCHANGE PROGRAM – 3 YEARS AND 43 TRANSPLANTS

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Introduction: Kidney paired donation has been at first performed at our institution in 2003. Until 2011 only four 2-way exchanges were performed. Czech national paired exchange program has been setup in 2011, based at singe/most experienced Czech transplant center. All the incompatible pairs are collected prospectively in the database. The computer matching run is performed every 3 months with on average 20 pairs included.
Methods: There were in total 43 paired live kidney transplants (KTx) performed in Czech since 2011. There were eight 2-way, two 4-way, two 5-way, two 6-way and one 7-way domino kidney paired exchanges performed, three altruistic samaritan donors entered the scheme so far. There were 9 (21%) cases of re-transplant, of those seven second, one third and one fourth KTx. Two surgeons performed all the transplants, one did all the mini-invasive nephrectomies using Hand Assisted Retroperitoneoscopic (HARS) live donor nephrectomy technique.
Results: Mean recipient age was 47.4 years (SD 11.8), eight patients had their second, one third and one fourth transplant done, mean SCr on discharge was 123.2 μmol/l (SD 40.3), equivalent of 1.39 mg/dl (SD 0.46). There was one case of delayed graft function, all the other 42 kidneys started to work immediately, 1 patient died 3 days after surgery from MI. The program did help some 42 patients so far, 4 more pairs are matched and will be transplanted shortly. The AB0i KTx program is being run in parallel as second option and also as a part of the program.
Conclusions: National kidney paired donation program can be run with the success in a single institution. Even long chains including 7-way exchanges can be performed at single institution. Paired donation limits some of the highly sensitized patients as well as blood group 0 recipients who may benefit from ABOi transplantation. To improve the matching rate, the cooperation with other European centers may increase number of incompatible pairs.

BO125* DUTCH EDUCATIONAL PROGRAMS HAVE EFFECT ON ORGAN DONATION

Jeantine Reiger, Michèle Van Beek, Maartje Puts
NTS

Purpose: Between February 2010 and September 2012 the NTS launched a line of educational programs on organ donation for youngsters between 10-20 years old. The goal is preparing youth for deciding about organ donation. Our study examined if DonorWise (secondary school) and Xtralife (occupational training) fulfil this goal.
Methods: The programs present neutral information; provoke opinion forming; urge discussion with contemporaries and families and stimulate registration of donor preferences: 'yes' or 'no'. Quantitative fieldwork: 317 students answered questions about their knowledge, opinion and behaviour towards organ donation before and after the lessons with the educational programs. In addition 898 teachers were questioned.
Results: The research shows positive effects. After lessons with DonorWise and Xtralife: students know more and say they know enough to make their own decision (increase of 20%). 17% of the students with no opinion before the lesson formed a stronger opinion afterwards. The programs show stronger impact on students at occupational training than at secondary school. After following lessons: more higher educated students are willing to donate (increase of 20%); they more often discussed donation with their friends and families; and 25% of them even intent or already have registered after the lessons. This is probably due to their higher average age (21 compared to 15 years old) and education level.
Conclusion: The educational programs DonorWise and Xtralife have a strong impact on the decision making process on organ donation. After lessons with DonorWise or Xtralife students are able to make a deliberate decision about organ donationand register their preferences more often than before the lessons.

BO126 AWARENESS AND PROMOTION OF ORGAN DONATION IN TEENAGERS – A VIDEO PROJECT APPROACH

Angie Scales
NHS Blood and Transplant

Background: Raising awareness of organ donation in teenagers.
Method: A funding application was made to support a video project as part of a community awareness initiative. Six 6th form students from one South East 6th form college ⟨150 students⟩ agreed to participate in promotional events and in addition a survey was circulated for input into design and format of the project. Input was also gained from donation and media teams regarding corporate aims of the project. Formal design storyboards were agreed in conjunction with Great Ormond Street Hospital ⟨GOSH⟩ and the chosen production company. Filming took place over 3 days with a specialist nurse–organ donation supporting throughout. Promotion agreed through GOSH/NHSBT websites, "You Tube", other suggestions being primary health care services electronic information screens and education programmes.
Results: 24 students completed the survey, return 16%, 96% stated the video would be useful.

Main ideas from students:

- Young people have a say.
- Music.
- Participants children.
- How donation can change lives.
- Who can donate and what.
- Life stories.
- Emotive messages.

Key corporate messages:

- Organ donation is a precious gift.
- Transplantation saves lives.
- Tell your family your wishes.

The video was formed of 3 sections– 2 recipients' stories/1 group discussion with consideration of minority groups. The final version was agreed and launched in conjunction with a national promotion week. It was promoted on the GOSH website, social media platform and "You Tube" a transcription also available. "You Tube" views on 14⁄3⁄15 –540.
Conclusion: The teenagers involved found it very interesting and thought provoking generating lots of discussion in their peer groups and requests for follow up sessions at the school. Wider dissemination of the material, incorporating NHSBT website and other social media platforms in conjunction with an education package would ensure maximum exposure to the target group.

BO127 SWEDISH INTENSIVE CARE NURSES ATTITUDES TOWARDS ORGAN DONOR ADVOCACY

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The concept of organ donor advocacy is critical to nurses who care for potential donors in order to facilitate organ donation (OD). Specific behavior among ICU-staff is significantly associated with consent to or decline of OD. This study emphasizes the importance of organizing the care of PODs and their relatives in a way that promotes advocacy.
Aim: To explore the attitudes of Swedish intensive care nurses towards organ donor advocacy.
Methods: A retrospective cross-sectional study was employed.Inclusion criteria in this survey were to be a registered nurse and to work in a Swedish intensive care unit (ICU). Participants were identified by the Swedish association of health professionals. A number of 502 Swedish ICU nurses answered the 32-item questionnaire Attitudes Towards Organ Donor Advocacy Scale (ATODAS), covering the five dimensions of organ donor advocacy.

Data were analyzed with the SPSS version 18.0 and the results were assessed by using Student's *t*-test and post hoc test, analysis of variance (ANOVA), X^2, Pearson's correlation and regression analysis.
Results: The most favored advocacy action was safeguarding the potential organ donors will and wishes by a professional approach, closely followed by actively and personally safeguarding the POD's will and wishes. Nurses at local hospitals reported a more positive attitude towards organ donor advocacy overall compared with nurses at larger regional or university hospitals. Important factors leading to positive attitudes were seniority, working experience, participating in conversations with relatives, caring for brain-dead persons and private experiences from OD or organ transplantation.
Conclusions: Intensive and critical care nurses with short working experience in university hospitals showed the least positive attitude towards organ donor advocacy. This is problematic because many ODs and all transplantations are performed in university hospitals.

BO128 IMPACT OF AN ON-LINE EDUCATIONAL PROGRAM TO HEALTH CARE PROFESSIONALS OF 11 CATALONIAN INTENSIVE CARE UNITS (ICU) ON END-OF-LIFE PRACTICES AND POTENTIALITY OF DONATION AFTER CONTROLLED DEATH (CDCD)

Alberto Sandiumenge[1], Mireia Llaurado[2], Nuria Masnou[3], Eva Oliver[4], Cebolla Maria Dolores Bosque[5], Mariona Badia[6], Maite Jurado[7], Gloria Miro[8], Elisabeth Navas[9], Marcos Ibañez[10], Marta Lopez[11], Beatriz Cancio[12], Teresa Pont[1], Pedro Lopez[13], Maria Bodi[14]
[1]U.H. Vall d Hebron, Barcelona; [2]University Rovira i Virgili, Tarragona; [3]U.H. Josep Trueta, Girona; [4]U.H. Bellvitge, Barcelona; [5]U.H. General de Catalunya, Barcelona; [6]U.H. Arnau de Vilanova, Lleida; [7]U.Hospital de Terrasa, Barcelona; [8]U.Hospital de Mataro, Barcelona; [9]U.H. Mutua de Tarrasa, Barcelona; [10]U.H Virgen de la Cinta, Tortosa; [11]U.H. Vic; [12]U.H. Moises Broggi, Barcelona; [13]OCATT; [14]U.H. Joan XXIII, Tarragona

Background: ICU professionals' lack of education on Life Support Treatment Limitation (LSTL) and cDCD may lead to misperceptions hampering the development of such actions. We aimed to assess the impact of LSTL and cDCD training on End-of-life care practices and potentiality for cDCD of 11 catalonian ICUs
Methods: Data on End-of-Life Care was prospectively collected before (P1: March-June 2013) and after (P2: Feb-May 2014) on-line training of 58 nurses and 62 doctors from the participating ICUs on LSTL and cDCD. Potential for cDCD was assessed through the analysis of clinical, analytical and agonal times (time from LSTL initiation to asystole) of patients in whom withdrawal of mechanical ventilation (MV) and/or vasoactive support (VAS) was performed as a form of LTSL
Results: A total of 6616 patients (P1:3315; P2:3301) were admitted with similar rates (P1:9.8%; P2:9.6%) and characteristics of patients undergoing LSTL between periods. Time from admission to First (5.19 ± 9.0 vs. 4.33 ± 8.94 days) and Definitive-LSTL (D-LSTL-the one preceding patient's death) (P1:$n = 215$; 6.83 ± 11.6 vs. P2:$n = 205$; 6.97 ± 11.0 days) were similar between periods. Futility (P1:74%; P2:73%), admission diagnosis (P1:62%; P2:50%) and co-morbidity (P1:40%; P2 45.9%) were the main causes for D-LSTL in both periods. Treatment withdrawal was the most common form of D-LSTL (P1:57.7%; P2:51.2%) ventilator support withdrawal being more frequent in P2 (80% vs. 67%) ($p < 0.05$). Sedoanalgesia was provided in 81% (P1) and 82.6% (P2) of patients in whom treatment was withdrawn. Agonal times after treatment withdrawal were shorter in P2 ($n = 105$) (115.0 min (25–75 ICR 37.0–405.0) compared to P1 ($n = 124$) (197.5 (25–75 ICR 55.0–675.0) ($p < 0.05$). Six (7.7%) and 4(5.5%) patients in whom VAS and MV was withdrawn during P1 and P2 could have been cDCD donors representing a 24% and 25% increase over the DBD donor pool respectively.

Conclusion: Although not influencing the potentiality of cDCD, training on LSTL improved End-of-Life practices.

BO129 EUROPEAN-MEDITERRANEAN POSTGRADUATE PROGRAM ON ORGAN DONATION AND TRANSPLANTATION (EMPODAT)

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Introduction: EMPODaT is a TEMPUS project (2013-2015) funded by the European Commission, Education, Audiovisual and Culture Executive Agency (EACEA). The consortium includes 11 partners from 4 European countries and 3 countries benefitting from the European Neighbourhood Policy Partnership Instrument (ENPI): Egypt, Lebanon and Morocco.
Objectives:

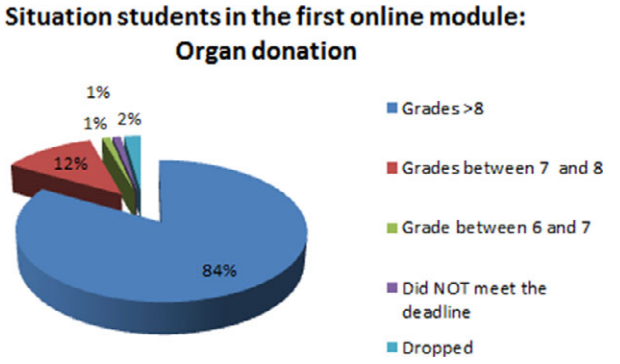
- To develop and implement a Postgraduate Program on Organ Donation and Transplantation (D&T) based on a common curriculum and certification degree, in accordance with the European Space for Higher Education.
- To train 12 ENPI tutors as faculty staff and coordinators of EMPODaT in their countries.
- To provide training to 90 ENPI students.
- To generate a consulting network.

Methods: EMPODaT consists of three main phases as follows:

- Design. The project started with a diagnosis study, based on which the consortium drew up the plan on how to create a homogenized EMPODaT curriculum.
- Development. A two level training program was developed: "Learn to teach" program aimed at training the ENPI Faculty Staff "Postgraduate Program" (750 h -30 ECTS) based on blended learning methodology: online modules, local seminars, practical hospital traineeships and international assessment seminars.
- Implementation and follow-up, currently in progress. Working language is English and French.

Results: 444 surveys were answered to identify the training needs on D&T in the ENPI partner universities. 12 ENPI tutors completed the ¨Learn to teach¨ course in Barcelona.

90 ENPI students were enrolled. Their results after the first online module are good (see below).



First online module was assessed by participants as follows: English version with 4.12 and French version with 4.15 2 on a scale from 1 (poor) to 5 (excellent).
Conclusions: EMPODaT may result in the development of safe and quality transplant systems in the Mediterranean area as the training of healthcare professionals is proved to have a positive impact upon organ donation.

BO130 THE APPLICATION OF THE DONOR ACTION PROGRAM MARKEDLY INCREASED DONOR RECOGNITION RATE REGARDLESS OF HOSPITAL SIZE

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Background: DAP (Donor Action Program) is a quality control program for identifying problems through the stages of brain death organ donation and finding solutions. DIP (Donation Improvement Program), which is a version of the DAP adapted for the condition of Korea, was applied from 2012, and this study analyzed the outcomes of its application for 3 years in order to see whether the recognition rate of potential brain dead organ donors was different according to hospital size.
Methods: This study reviewed and analyzed the medical records of 12 291 ICU patients (4163 in 2012, 4024 in 2013, and 4104 in 2014) who had died at 36 hospitals that operated DIP from January 1, 2012 to December 31, 2014.
Results: The number of PDs (potential donors) at the ICUs of the 36 hospitals where the program was applied was 1177 in 2012, 1,074 in 2013, and 1210 in 2014. The number of potential organ donors recognized by the medical staff and the number of actual organ donors were 276/87 in 2012, 362/128 in 2013, and 792/158 in 2014, so the recognition rate based on the number of PDs increased from 23% in 2012, the first year of the program, to 65% in 2014. According to the number of beds, the recognition rate increased from 25% in 2012 to 65% in 2014 among hospitals with 900 or more beds, from 23% to 73% among those with 600–900 beds, and from 15% to 37% among those with fewer than 600 beds. In addition, the brain death organ donation rate increased from 3% to 17% among hospitals with fewer than 600 beds (from 10% to 13% among those with 900 or more beds, and from 6% to 12% among those with 600–900 beds).
Conclusion: Although DIP was operated only for 3 years, the recognition rate and the donation rate increased in almost every hospital. This shows that, though the pool of potential donors is different according to hospital size, DIP is effective at all hospitals regardless of size.

019 ISCHEMIA/REPERFUSION INJURY/PRESERVATION

BO131 IMPACT OF HYPOTHERMIC OXYGENATED MACHINE PERFUSION (HOPE) ON FATTY LIVER GRAFTS

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Background: Liver transplantation (LT) is an effective treatment for end-stage liver disease. Despite worldwide success, however, organ shortage remains one major problem.Livers from extended criteria donors (ECD), i.e. donation after cardiac death (DCD) and steatotic liver grafts are therefore frequently used in many countries. However, ECD grafts are associated with a higher risk of dysfunction and inferior long-term outcome. Hypothermic oxygenated machine perfusion (HOPE) has been shown to protect liver grafts from biliary injury. Here we evaluate the impact of HOPE on steatotic grafts.
Methods: Rats were feeded over 4 weeks with methionine-cholin-deficient diet to induce severe macrosteatosis (>60%). Those livers were transplanted with either minimal or 24 hrs cold storage. Additionally, liver grafts were treated with HOPE for 1 h before transplantation. Reperfusion quality, liver function and injury, Kupffer - and endothelial cell activation, and amount of liver fibrosis were tested at different time-points (1 and 7 days, 4 weeks) after LT. Non-fatty livers served as controls.
Results: Implantation of steatotic liver grafts induced significant reperfusion injury compared to controls, which was further exacerbated by adding 24 hrs cold storage. While 1 h HOPE treatment after cold storage did not change the degree of steatosis, reperfusion injury decreased several fold by HOPE treatment, as detected by less enzyme release, less nuclear injury, and less Kupffer- and endothelial cell activation. Perfusion quality after LT was significantly improved by HOPE treatment. Untreated, cold stored steatotic grafts developed a significant fibrosis already 1 week after LT as compared to HOPE-treated grafts.
Conclusion: Besides its strong protective effects on DCD livers, HOPE is also potentially useful to ameliorate reperfusion injury in steatotic liver grafts. HOPE treatment therefore appears as an easy and practical opportunity to further expand the donor pool.

BO132 NORMOTHERMIC MACHINE PERFUSION OF CADAVERIC LIVER GRAFTS IS ASSOCIATED WITH IMPROVED POST-REPERFUSION HAEMODYNAMICS

Roberta Angelico[1], Thamara Perera[1], Reena Ravikumar[2], David Nasralla[2], Hynek Mergental[1], John Isaac[1], Garrett Roll[1], Ben-Hur Ferraz-Neto[1], Asim Iqbal[1], Hentie Cilliers[1], Suresh Vasanth[1], Paolo Muiesan[1], Peter Friend[1], Darius Mirza[1]

[1]Queen Elizabeth Hospital Birmingham; [2]Oxford Transplant Centre

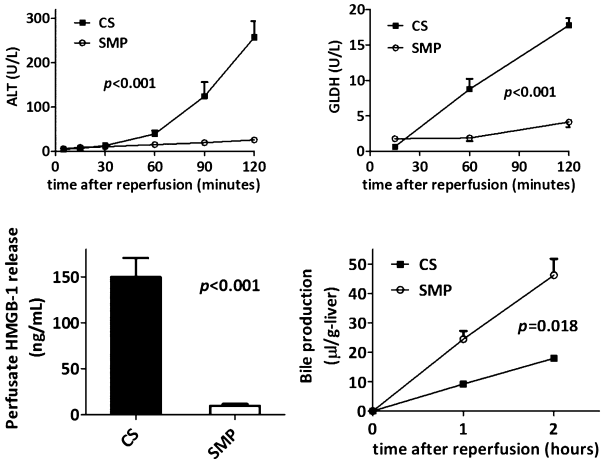
Background: Graft reperfusion poses a critical challenge during liver transplantation (LT) and can be associated with hemodynamic instability/post-reperfusion syndrome (PRS), which is sequel to ischemia-reperfusion injury (IRI). Recently, normothermic machine preservation (NMP) has been investigated as it mitigates the IRI, which is related with the severity of PRS and causes significant graft dysfunction in the early post-transplant. Herein we characterise haemodynamic changes related to PRS in liver grafts after normotherimc preservation and traditional cold preservation.
Material and Methods: Intra-operative records of patients receiving grafts after NMP ($n = 6$; NMPgroup) and cold storage ($n = 12$; CSgroup) were compared at the initiation of surgery, during hepatic dissection, anhepatic phase, at 5, 30, 60, 90 min after graft reperfusion. PRS was defined as mean arterial pressure (MAP) drop >30% of baseline, lasting for ≥1 min within the first 5 min from reperfusion.
Results: Donor, recipient, demographics and surgical parameters were evenly matched. NMP grafts were perfused for 9 ± 1.7 h after initial cold ischemic time(CIT) of 91(73–117)min, whilst in CSgroup CIT was 456(347–685)min; ($p = 0.001$). None developed PRS in the NMPgroup against $n = 2$ (16.7%) in CSgroup. NMP group had better intra-operative MAP at 90 min post-reperfusion ($p = 0.029$), achieved with a significantly less vasopressor requirement ($p \leq 0.05$) and less transfusion of blood products ($p = 0.030$) compared with CS group.
Conclusions: NMP is associated with a stable intraoperative hemodynamic profile post reperfusion, requiring significantly less vasopressor infusions and blood product transfusion after graft reperfusion, and may represent a better alternative to alleviate IRI in LT.

BO133 SUBNORMOTHERMIC MACHINE PERFUSION PRESERVATION OF >30% MACRO-STEATOTIC LIVERS; A NEW MEANS TO EXPAND THE DONOR POOL?

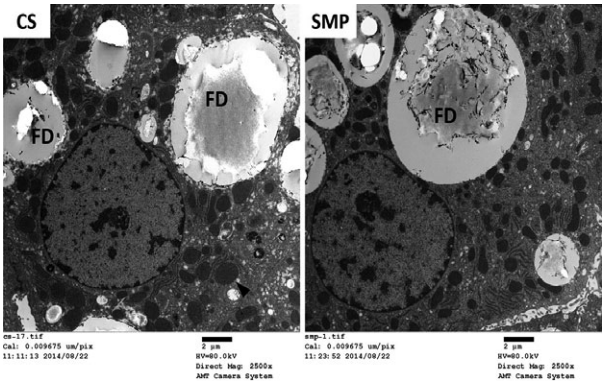
Yusuke Okamura[1], Koichiro Hata[1], Hirokazu Tanaka[1], Hirofumi Hirao[1], Toyonari Kubota[1], Osamu Inamoto[1], Kentaro Kadono[1], Shoichi Kageyama[1], Benedict M. Doorschodt[2], Rene H. Tolba[2], Shinji Uemoto[1]

[1]Division of Hepato-Biliary-Pancreatic Surgery and Transplantation, Kyoto University; [2]Institute for Laboratory Animal Science & Experimental Surgery, RWTH Aachen University

Background: The current drastic shortage of donor organs has led to increased acceptance of marginal livers for transplantation, despite higher risk of primary non-function (PNF). Here we report the impact of subnormothermic machine perfusion (SMP) preservation of >30% macro-steatotic livers, compared with the gold standard method, cold storage (CS).
Materials & Methods: Dietary hepatic steatosis was induced in Wistar rats (male, 250–270 g) by 2-day fasting and subsequent 3-day re-feeding with fat-free, carbohydrate-rich diet. This protocol induces 50-60% macrovesicular steatosis, which should be discarded when preserved by CS. Fatty livers were retrieved, flushed and preserved for 4 h either by CS in HTK or by SMP using modified-Polysol solution. In SMP, the livers were perfused both from the portal vein (1 ml/g-liver/min) and from the hepatic artery (0.1 ml/g-liver/min) at room temperature. Functional integrity of the grafts was then evaluated by oxygenated *ex vivo* reperfusion at 37°C for 2 h.
Results: SMP resulted in significant reduction of not only parenchymal (ALT: $p < 0.001$) but also mitochondrial (GLDH: $p < 0.001$) enzyme release. Moreover, PVP ($p = 0.047$), tissue ATP concentration after 2-h reperfusion (0.057 ± 0.002 μmol/g-protein vs. 0.041 ± 0.003 μmol/g-protein, $p = 0.001$), bile production ($p = 0.018$), HMGB-1 release (9.5 ± 2.3 ng/ml vs. 149.7 ± 20.8 ng/ml, $p < 0.001$), lipid-peroxidation and tissue glutathione content were all better preserved by SMP. Furthermore, electron microscopy revealed that SMP significantly alleviated deleterious alterations of sinusoidal microvasculature and hepatocellular mitochondria, both of which are characteristic disadvantages of steatotic liver grafts.



Conclusions: SMP could prevent PNF of 50–60% macro-steatotic livers, thus providing a new possibility to resuscitate discarded fatty livers for successful transplantation.



025 LIVER

BO134

OXYGEN CONSUMPTION IN HYPOTHERMIC AND SUBNORMOTHERMIC MACHINE PERFUSION OF HUMAN LIVERS

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University College London

Introduction: The data on oxygenated machine perfusion is very scarce in humans, and limited evidence has been shown on the dynamics of oxygen utilisation in different perfusion temperatures. The aim of this preliminary study is to compare the dissolved oxygen uptake, during oxygenated machine perfusion of human livers, performed at hypothermic and subnormothermic machine perfusion. To our knowledge this has not been presented before.
Methods: We analysed 6 discarded human livers, that underwent single-vessel machine perfusion through the portal vein, at 2 separate stages: hypothermic and subnormothermic perfusion. The perfusate used was KPS-1, and no oxygen carriers were added.

Dissolved oxygen profile was studies using 2 flow-through optical oxygen minisensors connected to an oxygen transmitter. The sensors were connected to the circuit at the portal vein and inferior vena cava (inflow and outflow consecutively). Measurements were taken every 3–4 s for 2 h, and the area under the curve was consequently calculated.
Results: The average oxygen consumption in the hypothermia group was 437.97 $\pm$ 134.53 μmol/ml/min, whereas the average oxygen consumption in the subnormothermia group was 429.86 $\pm$ 117.09 μmol/ml/min (Wilcoxon $Z = 0.314$, $p = 0.753$)

The average oxygen extraction ratio (OER) in the hypothermia group was 0.48 $\pm$ 0.22, whereas the average OER in the subnormothermia group was 0.65 $\pm$ 0.18 (Wilcoxon $Z = 2.201$, $p = 0.028$)
Conclusions: There was a non-significant effect of temperature ($p = 0.753$) on oxygen consumption in our experiments. We noticed a significant difference between the oxygen extraction ratio in hypothermic and subnormothermic perfusion ($p = 0.028$), and a strong effect size showing that 89.9% of the change in OER could be explained by the change in temperature.

019 ISCHEMIA/REPERFUSION INJURY/PRESERVATION

BO135 KIDNEY TRANSPLANTATION AFTER OXYGENATED MACHINE PERFUSION PRESERVATION WITH CUSTODIOL-*N* SOLUTION

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[1]University of Bonn; [2]University of Essen

Background: Custodiol-N, a new preservation solution designed to prevent free-radical induced tissue alterations and vascular patency of the graft, has been shown particularly suitable for hypothermic machine perfusion preservation (HMP) in isolated porcine kidneys. Now, these preliminary results should be confirmed in an actual porcine transplant model in vivo.
Methods: Kidney function after 21 h of HMP with a Lifeport Kidney Transporter was studied in an autotransplant model using Landrace pigs (25–30 kg; $n = 5$ per group). Perfusion was performed with oxygenation of the perfusate, using either Custodiol-N-solution including 4 g% of dextran 40 (CND) or kidney perfusion solution 1 (KPS1) as gold standard. Viability of the grafts was followed for 1 week after bilateral nephrectomy in the recipient pigs.
Results: HMP with CND resulted in less acute tubular injury, evaluated by levels of fatty acid binding protein and better Clearance function during the first 24 h after Tx than with KPS1 ($p < 0.05$,resp). Serum creatinine tended to be lower in the CND-group during the whole observation period. Fractional excretion of Na+, proteinuria and histological tissue scores 1 week after Tx were similar in both groups.Molecular tissue expression 15mn after reperfusion of endothelin-1 as well as toll-like receptor 4 was lower in the CND group ($p < 0.05$), suggesting less endothelial stress response; however no differences were seen with regard to von-Willebrand factor or endothelial nitric oxide synthase.
Conclusion: The data provide pre-clinical in vivo evidence for the suitability of Custodiol-N as an effective perfusate for renal machine perfusion in a large animal model.

BO136 EXTENDED DONOR HEART PRESERVATION USING A SINGLE-USE DEVICE BASED ON OXYGENATED HYPOTHERMIC PERFUSION

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[1]Paragonix Technologies Inc; [2]IPS Therapeutique; [3]Montefiore Medical Center

Background: Hypothermic machine perfusion has been used to extend the preservation time of donor organs. The *Sherpa Perfusion Cardiac Transport System* is a single-use device that provides oxygenated hypothermic puslatile perfusion (PP) to the heart. The purpose of the study was to compare the efficacy of this system to that of static cold storage (CS) in preserving the integrity and functionality of preserved porcine hearts.
Methods: Hearts recovered from Yorkshire pigs ($n = 4$/group) were assigned to a no ischemia group ("fresh"), static cold storage (CS) for 4 or 12 h at 4C, or perfusion preserved (PP) for 12 h at 4C. Celsior preservation solution was used in both treatment groups. A Langendorff, non-working heart system was utilized to assess functional and electrophysiologic parameters. The ability of the isolated hearts to resist reversible hypoxia was also tested.
Results: Left ventricular conduction intervals and contractility were similar in "fresh" and PP hearts, and alike those of 4 h CS hearts. 12 h PP hearts resisted hypoxia as well as 4 h CS hearts, while 12 h CS hearts exhibited intolerance to hypoxic conditions. Continuous coronary perfusion of 12 h PP hearts resulted in edema similar to that measured in 4 h CS hearts but less than that seen in 12 h CS hearts.
Conclusion: Hearts preserved for 12 h using oxygenated hypothermic machine perfusion showed similar functional characteristics to hearts preserved for the clinically accepted ischemic interval of 4 h. The perfusion technique employed here may therefore provide an extended period of *ex vivo* preservation allowing additional time for complicated recipient heart explants or consideration of geographically remote donors.

BO137 LUNGS FROM BRAIN-DEATH DONORS SHOW SIGNS OF CATABOLIC DISTRESS DURING EX-VIVO LUNG PERFUSION

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[1]Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico; [2]Ospedaliera San Paolo-Polo Universitario; [3]Dipartimento di Scienze della Salute, Università di Milano-Bicocca; [4]Clinica Medica AOUTS, Università di Trieste; [5]Azienda Ospedaliera San Paolo-Polo Universitario

Rationale: Lung metabolism in isolated human brain-death donors has never been investigated.
Objective: We assessed the kinetics of glucids, lipids and amino-acids in the perfusate during ex-vivo lung perfusion.
Methods: Lung perfusate was collected at 0, 60 and 240 min after reperfusion. Samples were analyzed by high-performance liquid chromatography to detect the concentrations of glucose, lactate, amino-acids, triglycerides, and cholesterol. De-novo synthesis and utilization of selected amino-acids were calculated.
Results: Ten brain-death donors were investigated. Before reperfusion perfusate contained glucose, albumin, traces of amino-acids, negligible amounts of lactate, and undetectable amounts of triglycerides and cholesterol; hematocrit was 4.9 $\pm$ 0.9%. During the course of the procedure, the concentration of glucose decreased (from 196 [181–200] mg/dl to 100 [91–102], 0 min vs. 240 min, $p < 0.05$) while lactate rose (from 0.9 $\pm$ 0.6 mmol/l to 13.0 $\pm$ 5.0, $p < 0.05$); the total concentration of amino-acids rose (from 201.9 $\pm$ 181.5 to 2279.2 $\pm$ 637.6, $p < 0.05$), among which phenylalanine, marker of catabolism (from 5.6 [2.1–6.1] to 82.2 [58.9–116.1], $p < 0.05$); triglycerides and cholesterol were not detected at any time. Leucine, isoleucine and lysine underwent utilization/oxidation, alanine and glutamine de-novo synthesis, while there was a clear shift from de-novo synthesis of glutamate at 60 min, to utilization/oxidation at 240 min.
Conclusions: Lungs procured from brain-death donors show signs of severe catabolic distress at reperfusion. Metabolism is active and dynamic during ex vivo lung perfusion; its modulation might foster lung function before transplantation.

BO138 EXPRESSION OF MIR-10A, -21, -29A, -221 AND -429 IN HYPOTHERMIC MACHINE PERFUSATE PREDICTS EARLY OUTCOMES IN KIDNEY TRANSPLANTATION

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Introduction: Hypothermic machine perfusion improves outcomes from kidney transplantation, and molecular analyses of hypothermic machine perfusate (HMP) have the potential to identify biomarkers of organ viability prior to transplantation. Effective prediction of organ-specific outcomes prior to transplantation offers enormous advantages to the transplant surgeon, and may increase the organ donor pool by allowing use of the ever-increasing 'extended criteria donors (ECD)'. MicroRNAs (miRNAs) have considerable potential for use as biomarkers of numerous pathological processes, including kidney disease. Our previous analysis of urine samples from renal transplant patients with delayed graft function identified miRNAs miR-10a, -21, -29a, -221 and -429 as potential biomarkers of kidney injury. This study aimed to determine if expression of these miRNAs predicted early transplant outcomes.
Methods: HMP samples were taken after 15 min, 1 and 2 h of perfusion for 11 kidneys (ECD/DCD) placed on the LifePort® prior to transplantation. Following RNA extraction using miRNeasy Mini Kits (Qiagen), cDNA was generated using the High Capacity Reverse Transcription kit (Life Technologies) and RT-qPCR was carried out using specific TaqMan microRNA detection assays (Life Technologies). Clinical data including demographics and eGFR at 6 months post transplantation were collected.
Results: MiRNAs were readily detected and found to be stable in the HMP medium from the 11 kidneys (ECD/DCD) included in this study. Expression of miR-10a, -21, -29a, -221 and -429 in HMP after 1 h of perfusion correlated significantly with eGFR at 6 months post transplantation.
Conclusion: MicroRNAs are emerging as important biomarkers in the context of kidney injury and transplantation. This study shows that expression miR-10a, -21, -29a, -221 and -429 in HMP is predictive of early outcomes following kidney transplantation. Further studies are underway to confirm these in larger cohorts.

BO139* DECIPHERING THE DE NOVO METABOLISM OF KIDNEYS DURING HYPOTHERMIC MACHINE PERFUSION USING ISOTOPIC NMR TRACER STUDIES

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Background: We have previously identified, using metabolomic NMR studies, a panel of metabolites present in the perfusate of human and porcine kidneys during Hypothermic Machine Perfusion (HMP) (1,2). We aim to determine the degree of *de novo* metabolism by incorporation of ^{13}C labelled glucose in the perfusion fluid of porcine kidneys.
Methods/Materials: Following organ harvest, porcine kidneys were subject to 6 h of HMP using the LifePort device. Glucose enriched with the non radioactive heavy carbon isotope in all six carbon positions ($U^{13}C$ glucose) was incorporated into the KPS-1 like perfusion fluid at a concentration of 10 mM. Analysis of perfusate and tissue extracts was performed using 2D Heteronuclear single quantum coherence NMR spectroscopy (2D-HSQC). The metabolic activity was then studied by quantifying the proportion of key metabolites containing ^{13}C.
Results: As expected, after 6 h of HMP there was a significant quantity of ^{13}C labelled lactate present in the renal cortex cell extracts (10.5%) and perfusate (5.31%). However, the presence of labelled alanine (5.14%), glutamic acid (0.08%), glycine, acetic acid and malonic acid were also demonstrated (Fig. 1). Increased ratios of labelled metabolites were observed as perfusion temperature increased and with supplemental oxygen (results not shown).
Conclusion: This study confirms the occurrence of de novo metabolism during HMP and highlights active metabolic pathways in this hypothermic hypoxic environment. The presence of non glycolytic pathway derivatives suggest that metabolism during HMP is more complex than previously appreciated. Isotopic Krebs cycle derivatives such as glutamic acid demonstrate that sufficient oxygen is dissolved in perfusate to facilitate some aerobic metabolism. Isotopic labelled *ex vivo* organ perfusion studies using 2D-NMR are feasible and informative.
References: 1) Guy, A.J., et al. *Transplantation* 2014 Sep 12.
2) Nath, J., et al. *PLoS One* 2014. 9(12): p. e114818.

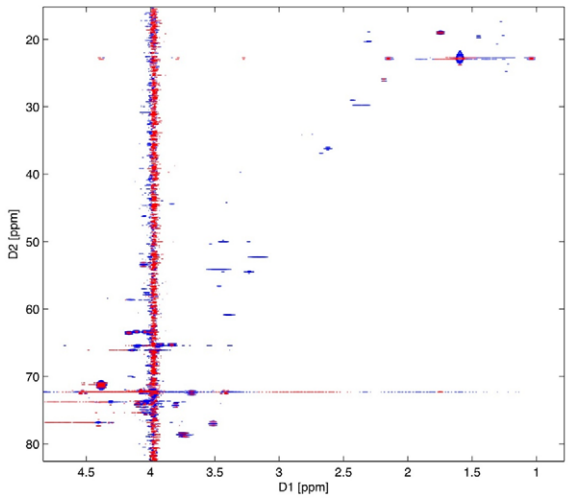

Fig. 1 Region from 2D HSQC spectra of perfusate after 6hrs of HMP demonstrating presence of multiple 13C labelled metabolites.

BO140 PRELIMINARY RESULTS OF ISOLATED ISLETS AFTER HYPOTHERMIC MACHINE PERFUSION OF HUMAN DONOR PANCREATA

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Background: Islet transplantation is an effective treatment option for patients with type I diabetes mellitus. Due to the persistent organ shortage, pancreata from marginal donors are more frequently used for islet transplantation. The conventional preservation method cold storage (CS), inadequately prevents ischemia prior to islet isolation. It is hypothesized that hypothermic machine perfusion (HMP) improves the quality of pancreata for islet isolation.

Methods Human donor pancreata unsuitable for clinical transplantation were connected to our modified dual arterial kidney machine system after an initial period of cold ischemia during transport. Islets of Langerhans were isolated after 6 h of oxygenated HMP. Islet viability was analyzed by fluorescein diacetate (FDA) and propidium iodide (PI) staining. Islet viability was analyzed by performing a glucose stimulated insulin secretion (GSIS) test. After 3 or 4 days of culture, the islets were transplanted under the kidney capsule in STZ-induced diabetic mice (3000 IEQ/mouse). Blood glucose levels were monitored every other day for 28 days.
Results: So far, three DCD pancreases have been included in this study. The preliminary data show an IEQ after isolation of 336957 $\pm$ 91019 and an IEQ/gram of 4476 $\pm$ 1785. Islet viability at day 1 was 98 $\pm$ 0% and at day 3 92.6 $\pm$ 4.6%. Static GSIS at day 1 showed an induction fold of 2.04 $\pm$ 0.42 and at day 3 2.57 $\pm$ 1.52. After transplantation, normoglycemia was achieved in 6 out of 10 mice. In 2 out of 10 mice, blood glucose levels normalized initially, but the graft function declined 14 days after transplantation. 2 out of 10 mice were terminated because of postoperative complications and early graft failure.
Conclusion: The preliminary data suggests that functional, viable islets can be readily isolated from pancreata after HMP. Inclusion of additional pancreata in the HMP preserved group and in a CS preserved control group is ongoing.

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BO141 LAPAROSCOPIC SLEEVE GASTRECTOMY AS A TREATMENT OF MORBIDLY OBESE PATIENTS PRIOR TO WAITLISTING FOR RENAL TRANSPLANTATION

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Background: The prevalence of obesity and obesity related morbidity in end-stage renal disease patients is rising. While it is established that obesity does not negatively influence the benefit achieved through transplantation with respect to lower long-term mortality and cardiovascular risk, obesity is associated with increased graft failure, delayed graft function, surgical site infection, prolonged hospital stay and costs.
Methods: We herein report a two step approach for morbidly obese renal transplant candidates. Patients with end-stage renal disease and a BMI of 35 kg/m^2 or higher underwent laparoscopic sleeve gastrectomy. After sustained weight loss and a BMI of <35 kg/m^2, patients were waitlisted for kidney transplantation.
Results: Laparoscopic sleeve gastrectomy was performed in 7 morbidly obese renal transplant candidates with a mean BMI of 38.6 kg/m^2. BMI dropped below 35 kg/m^2 within a median of 3 months. Excess body mass index loss (EBMIL) was 67.6% at 1 year after the bariatric procedure. Within a mean of 18 months from bariatric surgery five patients underwent successful kidney transplantation with good renal function and a serum creatinine of 1.9 ± 0.9 mg/dl at discharge. Two patients are waitlisted for transplantation.
Conclusion: Laparoscopic sleeve gastrectomy may be a safe and efficacious weight reduction strategy in morbidly obese renal transplant candidates. Rapid weight loss and subsequent waitlisting fo kidney transplantation may reduce the overall and in particular the post-transplant patient morbidity.

BO142 BARIATRIC SURGERY IN OBESE RENAL TRANSPLANTS: SINGLE CENTER EXPERIENCE

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OTC

Introduction: Obesity has been associated with poor graft and patient survival after kidney transplantation, requiring functional increase of anti-rejection drugs. Weight loss surgery may be a good alternative in this clinical scenario. The aim of this report is to assess the outcomes of bariatric procedures performed in patients after renal transplantation compared to conventional group of patients.
Patients and Methods: In this retrospective study, collected database was conducted to analyze the outcomes of obese patients after kidney transplantation (BMI>38) who underwent bariatric procedures during the last 5 years (n = 25cases) in comparison to controlled obese group without this type of surgery (n = 41 cases). Roux-en-Y gastric bypass was the most common procedure. We aimed to evaluate this type of surgery among renal transplant patients in comparison to control group.
Results: The two groups of patients were matched regarding their demographic data, type of donor, cases with IHD, type of induction and maintenance of immunosuppression. Most of patients in bariatric group were females (60%) while males dominated the other group (84%, p = 0.03). The basal and last follow up BMI means were 38.3 ± 8.9 and 33.3 ± 7.3; while they were 44.2 ± 5.6 and 44.2 ± 6.7 in the control group. The mean percentage of excess weight loss at 6 months in bariatric group was 15.4 ± 5.1% vs. 0.4 ± 0.2% in the control group (p0.05). There were no postoperative complications except in two patients: one with strangulated hernia; and the second with postoperative deep venous thrombosis and pulmonary embolism.
Conclusion: Bariatric surgical techniques may be used safely and effectively-with some precautions- to control obesity among renal transplant recipients. Further improvement in metabolic parameters and long term patient and graft outcome can be observed only with longer and larger studies.

BO143 EFFECT OF OBESITY ON RENAL TRANSPLANT OUTCOMES: A SINGLE CENTRE EXPERIENCE

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Royal Free Hospital Foundation Trust

Background: Obesity is a controversial issue when evaluating access to renal transplantation. Obese dialysis patients have an increased survival benefit after transplantation, but uncertainty remains as to whether obesity correlates with inferior outcomes post-transplant. Our aim was to determine the influence of obesity on transplant outcomes in our centre.
Methods/Materials: We retrospectively analysed 502 consecutive adult kidney transplants performed at the Royal Free Hospital between April 2009 and December 2013. 181/502 (36.05%) were live-donor transplants. Body mass index (BMI) was recorded at the date of transplant, patients with BMI >30 kg/m^2 were considered to be obese. Study end points were delayed graft function (DGF) and 1-year graft and patient survival. Logistic regression was used to investigate links between BMI and the study end points, correcting for potential confounding variables.
Results: 10 patients were excluded due to absence of a recorded BMI. Median recipient BMI was 25.4 kg/m^2 (range 13.3–41.1). 92/492 patients (18.7%) were obese. Recipient BMI category and race are shown in figures 1 and 2, respectively. DGF occurred in 41/92 obese recipients (44.5%), compared to 143/400 non-obese recipients (35.8%). Age, gender, operative time, and obesity were not significant factors for DGF. Black ethnicity and longer warm and cold ischaemic times were statistically significant factors for DGF (p = 0.036; p = 0.003 and p = 0.0001 respectively). Overall 1-year graft survival was 94.5%, with no statistical difference between obese (95.7%) and non-obese (94.3%) patients (p = 0.393). Overall 1-year patient survival was 96.7%, with no statistical difference between obese (96.7%) and non-obese (96.8%) patients (p = 0.388).

Figure 1. Recipient body mass index (BMI) category (percentages shown)

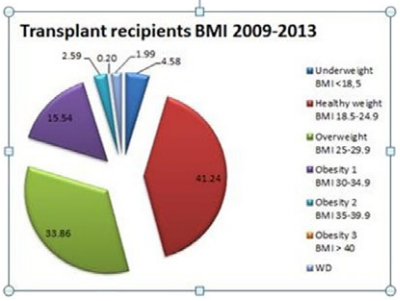
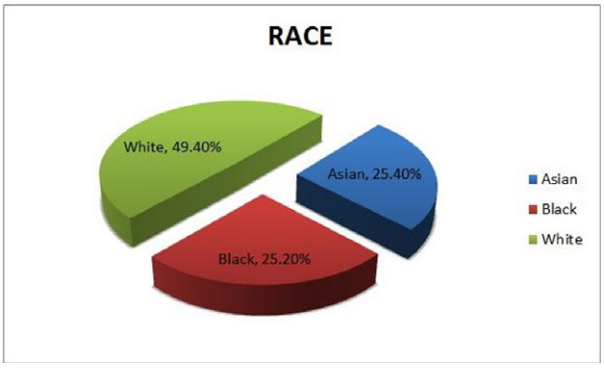


Figure 2. Recipient race



Conclusion: In our centre pre-transplant obesity has no impact on the rate of DGF, graft or patient survival at 1 year, when compared to patients with BMI <30.

BO144 RENAL TRANSPLANT OUTCOMES IN THE OBESE PATIENT

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Background: Morbid obesity is considered a relative contraindication to renal transplantation. Locally, we have adopted an inclusive approach. We aim to describe our outcomes with reference to BMI.
Methodology: A retrospective analysis of all renal transplants performed over a 10-year period was performed (n = 1005). Data were collected on graft and patient outcomes, peri- and post-operative complications and weight change in the year following transplantation. The association between these factors and BMI at time of transplantation was assessed.
Results: Mean recipient BMI at time of transplantation was 25.9 ± 4.8 kg/m^2. 15.5% had BMI 30–34.9 kg/m^2 and 4.3% had BMI ≥35 kg/m^2. There was no significant change in mean BMI year-on-year between 2003 and 2013 however the numbers of patients with morbid obesity has increased. Mean weight gain in the first year post-transplantation was 3.5 ± 1.4 kg. Patients with BMI <20 demonstrated the greatest weight gain (p < 0.001). BMI had no significant impact on 1-year graft or patient survival. Patients with BMI <20 kg/m^2 had a significantly higher eGFR than patients with BMI ≥20 kg/m^2 at 90, 180 and 365 days (p = 0.001). There was no significant relationship between BMI and eGFR at higher BMI. Wound complications (and more severe wound

complications [Clavien Dindo classification]) were more likely in patients with higher BMI ($p < 0.001$). Patients with higher BMI also spent significantly longer in hospital post-transplantation ($p = 0.02$). There was no association between BMI and the development of NODAT.
Conclusions: These results indicate that renal transplantation in the obese is safe with comparable 1-year graft and patient outcomes to the general population. Based on this evidence, patients with high BMI should not be excluded from transplantation. High rates of wound complications and longer length of hospital stay mayhave implications for resource allocation in transplantation of the obese patient.

BO145 EFFICACY AND SAFETY OF GASTRIC BALLOON IN OBESE PATIENTS CANDIDATES TO RENAL TRANSPLANTATION

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[1]APHP, INSERM; [2]APHP

Background: The number of obese patients candidates to a renal transplantation are considerably increased. The complications in immediate post transplantation are more severe and frequent. The weight loss is often difficult with a simple dietary. We have studied the efficacy and tolerance of intragastric balloon (BIG) in obese patients which are dialyzed and candidates to a renal transplantation.
Patients and Methods: Obese patients (BMI >30 kg/m^2) candidates to a renal transplantation are included prospectively. The placing and the removal of BIG were performed during gastric endoscopy with general anesthesia. The period of the treatment was 6 months. The end point was the decrease of BMI after 6 months. Impedancemetry, homa-test, nutritional status, energetic consumption, quality of life have been evaluated initially and after the removal of BIG.
Results: 17 (9 females and 8 males) with a median age of 53 years [40–72] have been included. The reduction of body mass index (BMI) during the 6 months was 4 kg/m^2 (37 (30–44.5) vs 33 (29–42) kg/m^2). The mean weight loss was 7 kg. The waist size decreased from 121 (136–109) cm to 114 (124–99). Patients lost mostly fat mass (from 43.6 to 40.6 kg/m^2) and this decrease remains stable 6 months after the removal of BIG. The tolerance was good without complication. The analysis of the other parameters are in process.To conclude, the efficacy of BIG in dialyzed patients candidates to a renal transplantation is similar to BIG in obese patient without renal failure and was well tolerated. BIG in obese patient candidates to renal transplantation can be used to decrease their body weight and facilitate their accessibility to renal transplantation.

BO146 BODY MASS INDEX; SHORT AND LONG-TERM IMPACT ON KIDNEY TRANSPLANTATION

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Background: The aim of this study was to investigate the influence of pretransplant BMI on short and long-term outcomes in patients receiving kidney transplant.MEHODS/MATERIALS:We have been analyzed 521 renal transplant recipients (RTRs) transplanted between January 1990 and February 2014.
Results: The RTRs were stratified into four groups according to the pretransplant BMI values: ≤20 (14.4%), more than 20 to ≤25 (50.9%), more than 25 to ≤30 (26.9%) and more than 30 (7.9%). There was no difference in the rates of delayed graft function between the four analyzed groups of patients. RTRs with normal pretransplant BMI were less likely to develop wound complications in comparison to the RTRs with high BMI (4.2% vs. 10%; $p = 0.04$) and obese RTRs (4.2% vs. 22%; $p = 0.0001$). Additionally, RTRs with normal BMI were less likely to develop lymphoceles in comparison to the RTRs with high BMI (12.8% vs. 27.9%; $p = 0.0003$). Obese patients were more likely to develop lymphocele in comparison to the RTRs with high BMI (48.8% vs. 27.9%; $p = 0.01$). The frequency of lymphocele occurrence is increasing as BMI is increasing (p for trend=0.003). Obese RTRs had longer mean length of hospital stay in comparison to the RTRs with normal BMI (44.6 ± 26.8 vs. 36.6 ± 22.7; $p = 0.04$). 45.3% of RTRs with low BMI, 59.2% of RTRs with normal BMI, 65.7% with high BMI and 70.7% of obese RTRs were readmitted in the year following kidney transplantation. There was no significant difference due to 1-year graft and patients' survival between the four investigated groups of recipients. We didn't found any significant difference in 5-years patients' and graft survival between the two subgroups of RTRs (those with BMI more than 20 to ≤25 and to those RTRs with BMI >25).
Conclusion: According to our experience overweight and obese transplant candidates should not be excluded from kidney transplantation.

BO147 INSULIN SENSITIVITY BEFORE AND 6 MONTHS AFTER KIDNEY TRANSPLANTATION

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Background: Severe uraemia is a known cause of insulin resistance which is an important factor in developing diabetes mellitus. Following kidney transplantation (Tx) the ureamic state is diminished but the risk of new-onset diabetes mellitus increases. We aimed to investigate the effect of kidney Tx on peripheral and central insulin sensitivity.
Methods: Nine non-diabetic patients awaiting living related kidney Tx were examined prior to Tx (Pre-Tx) with an oral glucose tolerance test (OGTT) and a 3 h hyperinsulinaemic euglycaemic clamp. The clamp was repeated 6 months after Tx (Post-Tx). Nine age, gender and BMI matched individuals with normal kidney function were examined once with an OGTT and clamp serving as controls (Ctrl). In six patients with corresponding controls the endogenous glucose production (EGP) and the glucose disappearance were measured by stable isotope tracer technique. Results are in mean [95% confidence interval].
Results: Two patients had pre-Tx prediabetes whereas all other had both normal fasting plasma glucose and normal glucose tolerance.The amount of glucose utilized during the clamp (average glucose infusion rate) was non-significantly lower in patients before Tx (Pre-Tx: 15.1 [11.2–19.0], Ctrl: 20.2 [13.4–27.0] μmol/kg/min, $p = 0.17$) but significantly reduced after Tx (Post-Tx: 9.8 [6.7–12.9] μmol/kg/min, $p = 0.01$). The suppression of EGP during clamp were comparable before Tx (Pre-Tx: 7.0 [5.4–8.5], Ctrl: 7.0 [1.3–12.7 μmol/kg/min, $p = 0.99$) but was significantly impaired after Tx (Post-Tx: 9.4 [7.8–11.1] μmol/kg/min, $p = 0.04$). The average glucose disappearance during clamp were comparable both prior to and after Tx (Pre-Tx: 18.1 [13.6 – 22.5], Ctrl: 22.3 [15.1 – 29.5], Post-Tx: 17.1 [13.4 – 20.8] μmol/kg/min, $p > 0.22$)
Conclusion: Reduced insulin sensitivity after kidney Tx is mainly due to central insulin resistance with impaired suppression of the endogenous glucose production and comparable peripheral insulin sensitivity.

BO148 VITAMIN D STATUS AND BONE HEALTH IN KIDNEY AND LIVER TRANSPLANT RECIPIENTS PERITRANSPLANT AND 6 MONTHS POSTTRANSPLANT

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Background: Inadequate vitamin D levels are highly prevalent in patients with end-stage organ failure.
Methods/Materials: Standardized, centralized measurement including bone turnover markers of prospectively collected samples (70 kidney and 70 liver recipients within the STCS) was performed. 25-OH vitamin D (25OHD) levels were classified as severe deficiency (<30 nmol/l), deficiency (>30&<50 nmol/l), suboptimal (>50&<75 nmol/l) and adequate (>75 nmol/l).
Results: Peritransplant and at 6 months posttransplant (post-TPL) the majority of kidney recipients had severely deficient 25OHD levels (45.7% resp. 31.4%). 27.1% resp. 34.3% had deficient levels, whereas a low proportion had suboptimal (15.7% resp. 30%) or adequate (11.4% resp. 2.9%) levels. 25OHD levels did not differ peri- and posttransplant, whereas 1,25-OH vitamin D (1,25OHD) was significantly higher at 6 months post-TPL, resulting in an increased ratio of 1,25OHD/25OHD (both $p < 0.001$). 85.7% had abnormal parathormone (PTH) levels peritransplant, this proportion decreased to 52.9% at 6 months post-TPL ($p = 0.001$). Correspondingly, CTx, a marker of bone resorption, but also P1NP, reflecting osteogenesis, significantly dropped after 6 months ($p < 0.001$). Comparably, at time of transplantation as well as

6 months post-TPL the majority of liver transplant recipients showed severe deficiency (51.4% resp. 45.7%) or deficiency (24.3% resp. 25.7%), only 12.9% resp. 14.3% had suboptimal and 11.4% resp. 2.9% optimal 25OHD levels. No significant change was recorded in 25OHD, 1,25OHD and PTH over time. Of note, CTx- as well as P1NP-values were significantly higher at 6 months post-TPL, resulting in a larger proportion of pathological results ($p = 0.002$ resp. 0.001).
Conclusion: Vitamin D deficiency is very prevalent at time of transplantation and at 6 months post-TPL. 6 months post-TPL improved renal hydroxylation results in increased 1,25OHD levels in kidney recipients and reduced bone turnover. In contrast, elevated bone turnover at 6 months post-TPL is observed in liver recipients.

BO149 PREDICTIVE MODEL FOR NEW ONSET DIABETES IN RENAL TRANSPLANT RECIPIENTS

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King Faisal Specialist Hospital

Kidney transplantation has shown to improve quality of life, morbidity and mortality. however, these patients are at increased risk of long-term complications including diabetes. Unfortunately, many patients develop New Onset Diabetes after Transplantation (NODAT). Previous studies have identified various risk factors for NODAT but to date no predictive model has been developed, which help identify such patients, councel them and may help to reduce the risk. We aimed to identify risk factors develop predictive model for NODAT.This is a single centre retrospective study of all adult kidney transplant recipients who received a kidney transplant between January 2003 to December 2009. Multivariate logistic regression analyses were used. 136 patients (27%) out of 500 developed diabetes (NODAT group). Older age (OR 1.06), family history of diabetes (OR 1.09), Hepatitis C infection (OR 1.92) and impaired glucose intolerance (OR 1.79) were found to be significant risk factors for the development of NODAT.Based on multivariate analysis, we have developed following predictive model:Risk = (1 + e-h)-1Where h is calculated as follows:h = −5.1987 + 0.0529(age) + 0.1058(Family history*) + 0.7524 (impaired glucose tolerance*) + 0.5892(HCV infection*) * "1" for positive and "0" for negative.
Conclusion: For the first time we have developed a model to predict diabetes in renal transplant recipients. This study has shown that around quarter of patients develop new onset diabetes after transplantation. Older age, family history of diabetes, impaired glucose tolerance and hepatitis C infection were identified as risk factors for the development of NODAT.

BO150 IMPACT OF PROTON POMP INHIBITORS ON HYPOMAGNESEMIA AND ARTERIAL STIFFNESS IN RENAL TRANSPLANT RECIPIENTS

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Background: Hypomagnesemia predicts cardiovascular morbidity and mortality in the general population and accelerated loss of kidney function in renal transplant recipients (RTRs). Proton pomp inhibitors (PPIs) or H2 receptor blockers (H2RBs) are frequently used agents after RT. The aim of this study was to evaluate the effects of PPIs on serum magnesium levels and arterial stiffness in RTRs.
Materials and Methods: We performed a study of 354 maintenance RTRs (mean age: 38.6 ± 10.7 years) with stable allograft function who had received their transplant at least 36 months previously. According to using stomach-protecting agents (SPAs), patients were divided in to three groups: PPIs (Group 1, *n*: 164), H2RBs (Group 2, *n*: 96) and control group who don't receive SPAs (Group 3, *n*: 94). Clinical and laboratory parameters were noted from recorded data. Estimated glomerular filtration rate (eGFR) was calculated by using the MDRD4 equation. Pulse wave velocity (PWv) was determined from pressure tracing over carotid and femoral arteries using the SphygmoCor system.
Results: Mean serum magnesium levels were significantly lower in group 1, however similar in group 2 and 3 (1.5 ± 0.04 mg/dl, 1.7 ± 0.02 mg/dl and 1.7 ± 0.01 mgdl, respectively). PWv values were significantly higher in group 1, whereas similar in group 2 and 3 (7.3 ± 0.2 cm/sec, 6.3 ± 0.1 cm/sec and 6.2 ± 0.1 cm/s, retrospectively). In linear regression analysis; type of SPAs (p: 0.001), serum calcium (p: 0.031), magnesium (p: 0.07) and folic acid levels (p: 0.013) were detected as the predictors of PWv.
Conclusion: We concluded that PPIs inhibit magnesium absorbtion independent from calcium metabolism in RTRs. Moreover, PPIs leads to increased arterial stiffness and cardiovascular risk in RTRs. Thus physicians should be aware of the side effects of PPIs to scale down the cardiovascular morbidity and mortality.

023 KIDNEY

BO151 TRADITIONAL AND NON-TRADITIONAL CARDIOVASCULAR RISK FACTORS, CAROTID INTIMA-MEDIA THICKNESS, ARTERIAL STIFFNESS AND PERIPHERAL ARTERIAL TONOMETRY IN STABLE KIDNEY TRANSPLANT PATIENTS

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Background: Chronic kidney disease is associated with accelerated atherosclerosis, arteriosclerosis, and endothelial dysfunction, which result in an increased risk of cardiovascular complications. There is limited evidence on the risk factors influencing the vascular injury in kidney transplant recipients. Thus, we performed a cross-sectional study to evaluate the role of traditional and novel or proposed non-traditional risk factors in the vascular and endothelial dysfunction in a large cohort of stable kidney transplant recipients.
Methods: One hundred-fourty-two kidney transplant recipients were enrolled into the study. Mean time after transplantation was 8.4 ± 1.8 years. Carotid intima-media thickness (IMT), pulse wave velocity (PWV), and peripheral arterial tonometry (RHI-PAT) were performed. The inflammatory markers, oxidative stress and endothelial function surrogate markers, adhesion molecules, as well as parathormone and osteoprotegerin levels were measured.
Results: Among traditional risk factors, only age, diabetes, left ventricular hypertrophy (LVH) and cardiovascular disease (CVD) were related to increased IMT and PWV, while RHI-PAT values were significantly decreased only in diabetics and patients with CVD and were similar in patients with and without LVH. There was no correlation between RHI-PAT values and plasma levels of asymmetric dimethylarginine (ADMA), endothelin 1, and adhesion molecules (VCAM-1 and ICAM-1).
Conclusion: In our cohort, age, diabetes, previous cardiovascular episode, and systemic microinflammation are predictors of vascular injury. Peripheral arterial tonometry is poorly associated with traditional CV risk factors, and does not correspond with levels of biochemical markers of endothelial dysfunction in stable kidney transplant patients.

BO152 OPTIMIZE THE REGISTRATION OF MALIGNANCIES IN RENAL TRANSPLANT RECIPIENTS; THE RESULT OF LINKING TWO DATABASES

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Introduction: Underreporting in the Dutch Organ Transplant Registry (NOTR) database may result in unreliable frequencies of malignancies after kidney transplantation. We investigated whether linking the national cancer database with the NOTR significantly alters this outcome.
Materials & Methods: The NOTR is operational since 2002 and includes the clinical data from recipients with a functioning organ transplant as reported yearly by the transplant centres. From 1989 onwards, the IKNL (Netherlands Comprehensive Cancer Organisation) collects nationwide pathology results documenting malignancy in a database. All renal transplant recipients (RTR), transplanted between 1966 and 2013, were connected with the malignancy database using surname, sex, date of birth, ZIP code and treatment hospital. Malignancy data of both databases were compared.
Results: The NOTR dataset consisted of 16717 RTR of which 3684 (22%) were diagnosed with a malignancy in the IKNL database. 1760 of these 3684 recipients had no documented malignancy in the NOTR database. The NOTR registers malignancies only during transplant follow-up. This results in missing data before transplantation (n = 581) and after organ failure (n = 169). Another 27% of the malignancies registered in IKNL was absent in NOTR for no good reason. 596 malignancies that were registered in NOTR were not in IKNL dataset probably due to matching difficulties. This changes the percentage of kidney transplant patients with a malignancy at follow-up from 15% in the NOTR to 21% with additional information from IKNL.
Conclusions: Linkage with the IKNL registry showed a significantly higher frequency of malignancies in RTR, due to underreporting in our national transplant registry. Transplantation is a known risk factor for developing malignancies but not per se diagnosed during follow-up of a functioning transplant. To add this information, future linkage with a unique patient identifier like citizen service number (BSN) is necessary.

BO153 THE SPECTRUM OF DE-NOVO CANCERS AFTER KIDNEY OR LIVER TRANSPLANT IN SOUTHERN EUROPE: EVIDENCE FROM A MULTICENTRE LONGITUDINAL INVESTIGATION IN ITALY

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Objective: To quantify, in Italy, the spectrum of de novo-tumors in Italians recipients of kidney (KT) or liver (OLT) transplant.
Methods: 9994 transplant recipients (67.1% males; 7224 recipients of KT, and 2770 recipients of OLT) were studied. The risk of cancer was assessed through sex- and age-standardized incidence ratios (SIR) computed by dividing the observed cases with expected ones from Italian cancer registries.
Results: Cancer was diagnosed in 701 study subjects (7.0%): PTLD (115 cases: 91 non-Hodgkin lymphoma – NHL), Kaposi sarcoma (KS, 92), and 526 solid tumors (lung, 76; head & neck, 61 -H&N; colon-rectum-anus 58, and prostate, 50). Significantly increased SIRs for all cancers were 1.7 in KT, and 1.5 in OLT. Statistically significant increased SIRs for both KT and OLT were found for KS (SIR = 97.9), PTLD (3.4) oral cavity (3.1) and solid tumors overall (1.3). Significantly elevated SIRs only in KT (eg, kidney) or in OLT (H&N) were also noted. Non significantly increased SIRs were also documented for adrenal gland (7.1), testis (2.8), melanoma (1.9) and lung cancer (1.3).
Conclusions: These study findings documented in southern Europe the elevated risk of cancer of KT or OLT recipients and the spectrum of neoplasms. Given the impact of virus-related cancers, particularly KS and PTLD, these observations strengthen the need of thorough control of infections in both the pre- and post- transplant period. *Members of the Study Group: G Grandaliano, M Rendina (Bari), MP Scolari, A Lauro (Bologna), S Sandrini (Brescia), GB Piredda, F Zamboni (Cagliari), M Veroux (Catania), A Famulari (L'Aquila); PG Messa, G Busnach (Milan), P Stratta (Novara), P Burra, P Rigotti (Padua), F Caputo, GB Vizzini (Palermo), Iaria M (Parma), GM Ettorre, G Tisone, M Rossi (Rome), MC Maresca (Treviso), L Biancone (Turin), U Baccarani (Udine), D Donati (Varese), C Cimaglia, D Verdirosi (INMI, Rome).

BO154 VENTRICULAR REPOLARIZATION HETEROGENEITY AND THE RISK OF SUDDEN CARDIAC DEATH AFTER KIDNEY TRANSPLANTATION

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Background: Sudden cardiac death (SCD) is the leading cause of mortality after kidney transplantation. We analyzed the value of ventricular repolarization heterogeneity (VRH) for prediction of SCD in kidney transplant recipients.
Methods/Materials: High-resolution 5-min 12-lead electrocardiogram and echocardiography were prospectively recorded in 68 consecutive non-diabetic kidney transplant recipients 1 year after transplantation. Beat-to-beat QT interval variability algorithm was used to calculate SDNN-QT and rMSSD-QT indices of VRH. To quantify QT interval variability relative to heart rate fluctuations, QTRR index was calculated. Left ventricular mass (LVM) index and presence of left ventricular hypertrophy (LVH) were assessed using two-dimensional M-mode echocardiography.
Results: After a median follow-up of 10.3 years, 14 patients (20.6%) died of SCD. At 1 year post-transplant, patient who died of SCD during follow-up did not differ with regard to previous time on dialysis, recipient age, gender, blood pressure, and estimated glomerular filtration rate as compared with control patients (64 vs. 58 months, 55 ± 10 vs. 53 ± 7 years, 64% vs. 55%, 133/83 vs. 131/81 mmHg, and 60 vs. 65 ml/min/1.73 m^2, respectively; $p > 0.05$). Indices of VRH, LVM index and incidence of LVH were significantly higher in patients who subsequently died of SCD as compared with control patients.

Parameter (at 1 year)	Sudden cardiac death (n = 14)	Control patients (n = 54)	p-Value
Ventricular repolarization heterogeneity			
SDNN (ms)	5.7 ± 3.8	3.8 ± 2.4	0.035
rMMSD (ms)	7.4 ± 4.2	4.2 ± 3.4	0.042
QTRR	0.11 ± 0.09	0.20 ± 0.11	0.012
Echocardiography			
LVM index (g/m^2)	147 ± 12	128 ± 26	0.010
LVH (%)	13 (93)	31 (57)	0.007

Receiver-operator-characteristic curve analysis demonstrated that SCD can be predicted with a sensitivity of 80% and a specificity of 71% with the use of a cutoff value of 0.13 for QTRR index, and with a sensitivity of 79% and a specificity of 76% with the use of a cutoff value of 135 g/m^2 for LVM index. In adjusted analysis, a QTRR index >0.13 and a LVM index >135 g/m^2were independently associated with SCD (HR 6.4, 95% CI 1.3–12.4; $p = 0.026$, and HR 7.1, 95% CI 1.4–17.5; $p = 0.017$, respectively).
Conclusion: Increased VRH and greater LVM index are predictive of SCD in kidney transplant recipients.

BO155 SUPERIOR VEINA CAVA SYNDROME IN RENAL TRANSPLANTS RECEIPIENTS: A 14-YEAR SINGLE CENTRE EXPERIENCE

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Introduction: Transplantation of patients with superior vena cava syndrome (SVCS) is typically associated with increased mortality and morbidity such as airway oedema and obstruction .The aim of this study is to evaluate the risk factors for developing SVCS and review local morbidity and mortality rates from SVCS in renal transplants recipients.
Methods: All recipients of renal transplant from live and deceased donors between 2000–2014 were included in the study. Magnetic resonance venography (MRV) was used to assess patients with superior vena cava occlusion or occlusion of other central veins eg, inominate veins. Patient data on demographics, ethnicity, primary kidney disease, and vascular access history, length of time on dialysis, thromboembolic events and anticoagulation were collated.
Results: Twelve patients were identified with SVCS (4 live donor, 8 deceased donor transplants). Mean age was 41.8 years (range 20–64). 7/12 patients (58%) were Afro-Caribbean. Length of time on dialysis varied from 1 to 32 years (mean 8.3 years). Six (50%) had severe parathyroid disease and 4/12 (30%) were on warfarin. Post transplant, there was one (8%) fatality due to sepsis and muti-organ failure. Two patients required post-operative tracheostomy, 5 required ITU stay. Mean length of hospital stay (LOS) was 18.5 days (range 7-45). LOS was shortened in patients with live donor transplant (7–9) .Pre-operative venoplasty was performed in 7 patients. Post-operative venoplasty was required in 5 patients.
Conclusion: Early identification of SVCS and pre-operative venoplasty may reduce morbidity and LOS in renal transplant recipients. MRV is a useful tool for assessing patients with suspected SVCS. Successful access surgery is needed to avoid the use of tunnelled central lines. Peri-operative strategies such as fluid administration via a femoral venous route and "headup" position may reduce airway oedema and therefore complications associated with renal transplantation in these patients.

BO156 INCIDENCE AND OUTCOMES OF POLIOMA-VIRUS ASSOCIATED NEPHROPATHY IN KIDNEY TRANSPLANTATION

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Background: BK viremia and BK virus-associated nephropathy is one of the important complications of kidney transplantation that leads to graft dysfunction and loss. BKV infection is associated with many other interactive factors and immunocompromised patients who have immunosuppressive therapy appear to be more increased BK infection. But risk factors for BK viremia are incompletely understood.
Methods/Materials: Between August 2010 and October 2012, 302 patients received kidney transplantation at our center. Tacrolimus, MMF and steroids were used for maintenance therapy. BK viuria and viremia were monitored with urine and blood BK virus PCR using our BK virus monitoring protocol. We divided 4 groups as BK status: no BK infection, BK viuria only, low BK viremia (<4 log unit), high BK viremia (more than 4 log unit) group. We reviewed medical records including biopsy and BK virus PCR in the patients.
Results: In 57 among 302 patients had BK viremia(18.9%) and 18 patients had BK nephropathy(5.9%) that were proven by biopsy during 2 years follow up period after kidney transplantation. Age, sex, number of human leukocyte antigen mismatches, CMV viremia, number of over than 50% PRA status, existing of DSA, type of transplantation, delayed graft function and hospital days were no significant difference between groups. In viuria and low viremia group, clearance of BK infection was better than high viremia group ($p = 0.001$) and duration of BK infection in high viremia group was more longer than low viremia group ($p = 0.002$). All BKV nephropathy was diagnosed in high BK viremia group (18/34, 52.9%). eGFR was significantly lower in BK viremia group than no BK infection group at 1 and 2 years after KT.
Conclusions: In recipients with BK viremia in blood PCR tend to worsening graft function during 2 years follow up. Long-term follow-up and controlled studies should be required for elucidating the risk factor of BK-virus infection and survival after kidney transplantation.

BO157 POST KIDNEY TRANSPLANT NEPHROCALCINOSIS

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Introduction: Renal allografts are at risk for calcium salt deposition. This nephrocalcinosis has been linked to kidney dysfunction and poorer graft outcome. Increased understanding of the prevelnce, causes and effects of nephrocalcinosis in the renal transplant population may aid in changes in practice and therapy that may aid in prolonging long term allograft survival.
Methods: We enrolled 100 incident kidney transplant recipeints to participate in a prospective study. As part of the routine care of trasplant patients in our program, renal function is assessed by iothalamate clearance in the early post transplant period then annually therafter. Protocol surveillance biospsies are also obtained at implantation, 4, 12, 24, 60 and 120 months post transplant irrespective or graft function. In addition to the routine care paitents receive at our institution, study patients underwent a 24 h urine collection to assess urine supersaturation 3 weeks post transplant and 1 year after. Study patients had a von Kossa stain performed on their biopsies. Here we present results of 53 patients whose 4 and 12 months biopsies have been scored.
Results: Mean age 52.7 ± 12.7 range 28–71 years. Males 30 (57%), 44 (84%) Caucasian, live donor recipients 45 (85%) and 31 received their kidney transplant without initiation of dialysis. Mean iothalamate GFR was 49 ml/min/1.73 m^2 at 3 weeks post transplant and 58 ml/min/1.73 m^2. At 4 months post transplant 19 (36%) patients had renal allografts with calcium crystals noted. Only one (5.3%) was caclium oxalate the remaining 18 (95%) had caclum phosphate. There was no difference in renal function at 1 year between those with crystals and those without. Urine volume, urinary calcium and phosphorus were no different between the two groups.
Conclusion: Renal allgoraft nephrocaclinosis is common. Predominately caclium phosphate with no demonstrable effect on renal function at this time within the first year post transplant.

BO158 KIDNEY TRANSPLANTATION PATIENTS FROM THE DECEASED DONOR WHO NEED CONTINUOUS RENAL REPLACE THERAPY (CRRT)

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Background: Acute renal failure (ARF) in previous healthy person is mostly reversible condition with recovery of underlying condition. Brain death donor may need CRRT in severe ARF during management. To maximize donor organ usage we performed renal transplantation from deceased donor who needs CTTR with informed consent. This single-center study reviewed the clinical outcomes of kidney transplant recipients from extreme marginal donors who need CRRT.
Methods: We retrospectively reviewed medical records in all patients used the graft from extreme marginal donors who underwent CRRT in AMC between June 2007 and September 2014.
Results: Between June 2007 and September 2014, we transplanted 27 kidneys from 19 CRRT donors. Mean donor age was 35.1 years (range 16–56 years), male donor was 14 (74%). The causes of brain death included head trauma in 6, hypoxia in 5, stroke in 4, and others in 4. The main causes of CRRT were anuria in 14, electrolyte imbalance or acidosis in 5, and mean duration of donor CRRT was 3.6 days (range 1–11 days). Delayed graft function (DGF) developed in 24 (88.9%) but all of them recovered renal function. After 11 days after transplantation they can be free from dialysis).But mean recipients' hospital stay was 30 daysMean serum creatinine level at 1 month, 1 and 5 year was 1.85 mg/dl, 1.26 mg/dl and 1.31 mg/dl respectively.
Conclusions: 5 years follow up data shows that renal transplantation from severe ARF donor has excellent outcome.Although CRRT donor kidney transplants have a higher rate of DGF, the presence of DGF, unlike other donation after brain death donor kidney transplants, does not portend a worse prognosis.

BO159 ELEVATED POST-TRANSPLANT CANCER INCIDENCE AND REDUCED SURVIVAL IN PATIENTS WITH PRE-TRANSPLANT TUMORS

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Background: Patients with previous malignancies have increasingly been accepted for renal transplantation. However, post-transplant cancer risk and survival rates in these patients have never been investigated. Our aim was to,

for the first time, systematically determine the fates of these patients and assess if previous cancer diagnosis pose an unnecessarily high risk of post-transplant tumors and the organs as a resource is too limited for investment in this patient group.
Methods: This retrospective, nested case control study assessed the outcome of 95 renal transplanted patients with a pre-transplant cancer diagnoses in the Uppsala-Örebro region. The control group was obtained from the Collaborative Transplant Study (CTS) registry and included European patients without pre-transplant malignancies at a 1:1 ratio (case:control) with patients from Uppsala and 1:3 ratio with patients from Europe. Development of recurrent and de novo tumors, patient survival, mortality due to malignancy and graft survival were analyzed by using Kaplan-Meier method.
Results: Patients with pre-transplant malignancies had higher standard incidence ratio of post-transplant malignancies and lower survival rates compared to the control groups ($p < 0.001$). Men had higher post-transplant malignancy rates and reduced survival compared to women. Overall cancer induced mortality reached a staggering 47% in the pre-transplant group. Graft survival was unaffected.
Conclusions: The risk of post-transplant cancer and mortality is higher than anticipated, sometimes too high, in patients with pre-transplant malignant tumors despite previously adequate cancer treatments and favorable prognoses. Grafts are not wasted. Therefore we recommend more cautious selection criteria and reintroduction of at least 2-year tumor free interval before renal transplantation.

BO160 WHY DO RENAL TRANSPLANTS FAIL? – A WELSH PERSPECTIVE

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Background: Maximising long term renal graft survival is a key aspect of transplant care. It is readily known that a return to dialysis adversely affects patient morbidity and mortality. In 2012, we undertook a study to investigate the factors leading to graft loss in a major UK transplant centre. This highlighted the issue of non compliance as a significant contributory problem which was particularly prevalent in young patients. We have now extended this study over a different time period and have included hospitals throughout Wales.
Method: A retrospective analysis was undertaken looking at contributory factors leading to graft loss over the 3 year period from January 2011 to December 2013. Data was collected from four hospitals throughout Wales.
Results: 103 graft failures were identified over a 3 year period. The prevalent transplant population in the four units is 1616. 72% of the failures occurred in men. Within the group, the median age at the time of transplantation was 42 years ($\pm$ 15) and the median age at the time of graft failure was 47 years ($\pm$ 15). Mean graft survival for the cohort was 8.2 years ($\pm$ 7). The majority of the patients had at least one biopsy to investgate the cause of graft dysfunction and 34% had a biopsy proven episode of rejection. Of these, at least 25% had a history of non compliance. 67% of these patients were the young recipients of living donor grafts. 28% of grafts failed due to 'chronic graft nephropathy' with recurrent IgA also featuring prominently. 72% of patients commenced haemodialysis following transplant failure and 36% of patients were relisted for a further transplant.
Conclusion: This extended study confirms that non compliance and subsequent immunological graft damage is a major cause of renal transplant loss. Young recipients of living donor kidneys are again emerging as a high risk group and our attention should be focussing on strategies to avoid this potentially avoidable cause of graft failure.

025 LIVER

BO161 THE OUTCOMES OF ADULT LIVING DONOR LIVER TRANSPLANTATION WITH SMALL-FOR-SIZE GRAFTS

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Background: Size mismatching is a major concern in adult living donor liver transplantation (ALDLT), because small-for-size (SFS) graft may increase a risk for SFS syndrome. Portal hyperperfusion is considered a primary factor of SFS syndrome, and portal vein pressure (PVP) control is widely performed. The aim of this study is to review our experience of ALDLT with SFS grafts.
Methods: Until July 2014, ALDLT was performed in 44 patients with 22 right lobe grafts (RL), 20 left lobe grafts (LL) and 2 posterior sector grafts. Among these patients, 22 received SFS grafts with actual graft-to-recipient weight ratio (GR/WR) 20 mmHg after the completion of all vessel anastomoses of the graft. Postoperative course was retrospectively evaluated. Results

Seven RL and 15 LL were SFS grafts. The mean actual GV, GR/WR and GV/SLV were 451 g, 0.67% and 36.6%, respectively. Thirteen patients underwent PVP control. The mean actual GV, GR/WR and GV/SLV of these patients were comparable to those of patients without PVP control. The mean final PVP was 20.1 mmHg and 9 patients had PVP > 20 mmHg despite performing PVP control. The prolonged cholestasis, intractable ascites and coagulopathy were observed in 12, 15 and 2 patients, which were similar incidence in patients with non-SFS grafts, while the average daily amount of ascites in the first 2 weeks after LDLT was higher in patients with SFS grafts than with non-SFS grafts. The overall 1- and 3-year patient survival rates in patients with SFS grafts were 86.4 and 86.4%, which were comparable to those in patients with non-SFS graft.
Conclusions: Although PVP control did not always reduce PVP <20 mmHg, the outcomes of ALDLT with SFS grafts were equivalent to those of ALDLT with non-SFS grafts. PVP is not the only factor determining the outcome of ALDLT.

BO162 INTRA-OPERATIVE HEPATIC FLOW MEASUREMENT IN LIVING DONOR LIVER TRANSPLANTATION: DOES IT REALLY AFFECT INFLOW MODULATION DURING TRANSPLANTATION?

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Introduction: Adequate liver perfusion is of significant importance for organ function after liver transplantation. We measured intra-operative arterial and portal blood flow and evaluated their effect on the potential inflow modulation during living donor liver transplantation (LDLT).
Methods: From March, 2014 to December 2014, a total of 74 LDLT recipients (41 adults; 23 males and 18 females, and 33 children; 17 females and 16 males) were prospectively assessed by measuring arterial and portal blood flow with a transit time ultrasound flowmeter.
Results: In the adult group. The median age is 58 years (range 17–73). The mean graft weight is 709 grams (range 400–1034); mean recipient portal blood flow is 1212 ml/min (range 440–2120) with recipient portal blood flow/graft weight ratio is 1.7 l/min (range 0.97–2.93). The mean arterial blood flow is 157 ml/min (range 90–375). In the pediatric age group. The median age is 19 months (range 4–111). The mean graft weight is 245 grams (range 120-396); mean recipient portal blood flow is 395 ml/min (range 159–973) with recipient portal blood flow/graft weight ratio is 1.6 l/min (range 0.8–3.97). The mean arterial blood flow is 107 ml/min (range 54–330). After portal and arterial reperfusion, 5 recipients (6.75%); 3 adults and 2 children developed portal hyperperfusion by more than 5 fold of the normal physiological value (100 ml/min/100 gram liver mass) and low hepatic arterial flow (<100 ml/min). After splenic artery ligation there was a significant reduction in portal blood flow with consecutive improvement in recipients' hepatic arterial flow.
Conclusion: Portal blood flow can be safely modulated by intraoperative splenic artery ligation. Intra-operative hepatic flow measurement is a useful monitoring and easy to apply. It can help to optimize hepatic perfusion and might become routine in LDLT.
Key words: Portal blood Flow – living donor liver transplantation – Inflow modulat

BO163* TEMPORARY XENOGENEIC TRANSPLANTATION TO REGENERATE SMALL FOR SIZE LIVER GRAFT

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Background: Live donor liver transplantation (LDLT) is hampered by small for size syndrome (SFSS). The ideal LDLT should be harvesting <30% liver from live donors, while transplanting more than 40% liver graft to recipient patients. To prevent SFSS and safer live donors and patients in LDLT, we proposes a novel strategy: auxiliary partial liver xenogeneic transplantation (APLXT) to regenerate small for size liver graft.
Methods and Materials: 30% liver grafts were harvested from C57/B6 mice, and then APLXT transplanted to 70% hepatectomized Lewis rats. Tacrolimus was applied as the suppressant. Liver grafts wereharvested at 2, 7 days after transplantation. The weight of liver grafts, H&E, immunohistochemistry staining, PCR, ELISA, were measured and performed for analysis. Liver grafts re-transplanted back to mice were performed after mouse-to-mouse syngeneic and mouse-to-rat xenogeneic transplantation.
Results: Recipient rats were survived till harvesting days. The mouse liver grafts showed hepatocyte mitosis and proliferation in H&E, PCNA and Ki-67 staining at day 2, and doubled their origin size at day 7 after APLXT. IL-6, TNF-a, HGF released dynamically different between liver graft and rat residual liver at early phase of APLXT. Anti-CD3 & CD68 staining were positive in mouse liver grafts at day 2 and 7 postoperatively. The liver grafts re-transplanting back to mice is feasible after the mouse-to-rat xenogeneic transplantation.
Conclusion: Small mouse liver grafts regenerate in rats and doubled their volume in 7 days after APLXT. Acute graft rejection was not observed under tacrolimus treatment. Regeneration pathway of mouse liver grafts was rat recipient-independent. Liver grafts re-transplant back to mice is feasible with sufficient function and permanent survival. However, sufficient liver graft regeneration is required for a successful re-transplantation. APLXT may increasing the rate of LDLT by a smaller hepatectomy risk of the live donor.

BO164 A PORTAL PRESSURE CUT-OFF OF 15 VERSUS A CUT-OFF OF 20 FOR PREVENTION OF SMALL-FOR-SIZE SYNDROME IN LIVER TRANSPLANTATION: A COMPARATIVE STUDY

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Background: Small-for-size liver graft injury in adult-to-adult living-donor liver transplantation (A-LDLT) can contribute to postoperative graft dysfunction known as Small-for-size syndrome (SFSS). Portal hypertension has recently been implicated in SFSS pathogenesis. We conducted a prospective observational study in order to compare the portal venous pressure (PVP) cut-off values of 15 mmHg and 20 mmHg in terms of prevention of SFSS in A-LDLT.
Patients and Methods: Thirty-three patients underwent A-LDLT between October 2009 and June 2013. A PVP <20 mmHg at the end of the operation was targeted using graft inflow modulation. Patients were divided into 2 groups; group A with final PVP <15 mmHg (n = 16) and group B with final PVP 15-19 mmHg (n = 17). We diagnosed postoperative SFSS on the basis of the Clavien definition.
Results: Final PVP was well controlled below 20 mmHg in all patients. Three patients suffered SFSS in group B (17.6%) compared to no patients in group A; p = 0.078. Four patients died in group B (23.5%), two of whom died of SFSS, compared to 1 patient in group A (6.2%); p = 0.166.
Conclusion: A PVP cut-off of 15 mmHg seems to be a more appropriate target level than a cut-off of 20 mmHg for prevention of postoperative SFSS in A-LDLT.

BO165 PERI-OPERATIVE FACTORS ASSOCIATED WITH A VARIATION OF SVV (STROKE VOLUME VARIATION) AFTER REPERFUSION OF ALLOGRAFTS DURING LIVING DONOR LIVER TRANSPLANTATION

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Background: Stroke volume variation (SVV) is a useful dynamic parameter as preload responsibility. SVV has recently been reported to its usefulness for fluid management during liver transplantation (LT). However, reported literature of SVV is limited to a response to administer fluids during operation, and has not been reported in research on perioperative factors except hypovolemia. The aim of present study is to propose clinical validity of a SVV by investigating a correlation between SVV and perioperative factors during LT.
Methods: The present prospective study was conducted 70 adult patients (age ≥19) undergoing living donor liver transplantation (LDLT) between March 2012 and March 2014 at Seoul St. Mary Hospital. SVV obtained from the FloTrac/Vigileo system during operation. The present study used SVV at 1 min

after allografts reperfusion on the data analyses. SVV at 1 min after reperfusion was dichotomized by its median value, and we were divided into two groups by dichotomized SVV (SVV ≤16%, $n = 32$; SVV >16%, $n = 38$). Patient data was analysed using a student's *t*-test or chi-squared as appropriate. Selected meaningful variables were analysed by binary logistic regression.
Results: Predictive model was deducible by the results of multivariable analysis using the expected variables to threshold value of 16% for SVV. Mean heart rate at dissection phase, and arterial oxygen content were analysed out, those raised the risk of high level of SVV at 1 min after reperfusion as 1.08 times, and 0.60 times respectively. Administered adrenaline dose to maintain hemodynamic stability at reperfusion, and right ventricular stroke work index at reperfusion also raised the risk as 5.29 times, and 0.76 times respectively.
Conclusions: The level of SVV at reperfusion correlated with perioperative patient hemodynamics. Thus, SVV at reperfusion contributes data that anesthesia provider can incorporate for hemodynamic management decision making.

BO166 IN-VIVO SPLIT LIVER TRANSPLANTATION FOR TWO ADULTS

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Background: Left lateral section graft for child and right trisection graft for adult were common type of split liver transplantation. Split liver transplantations for 2 adult were rarely reported. The purpose of this study was to examine the results of split liver transplantation for 2 adults in single center.
Methods: From 2003 to 2014, we performed 16 adults split liver transplantations from 8 deceased donors at our center. All donor operation was performed by in-vivo splitting technique. Middle hepatic vein was reserved in left liver graft side.
Results: All donors were male. Mean age of donors was 25.8 ± 9.8 years old and body mass index of donors was 25.52 ± 5.65. 8 recipients received right liver graft. 7 recipients received left liver graft. 1 recipient received dual donor liver transplantation with 2 left liver grafts (1 left liver graft from living donor). Mean age of recipients was 49.6 ± 7 years old. MELD score of recipients was 21.3 ± 8.6. Mean cold ischemic time was 345.6 ± 311.7 min. 1 year and 5 year graft survival were same as 75.0%. 1 and 5 year patient survival were same as 81.3%. Causes of death were sepsis ($n = 2$) and graft failure from heart dysfunction ($n = 1$). One graft failure was associated with primary non-function due to long cold ischemic time. There was 1 biliary complication in right liver graft recipient and 1 hepatic vein stenosis in right liver graft recipient. There was no arterial complication and small-for-size graft syndrome after split liver transplantation.
Conclusions: In-vivo split liver transplantations for 2 adults are feasible options for expanding door pools in selected cases.

BO167 THE EFFECTIVENESS OF THE MOVING TO MORPHINE AUGMENTED MAGNETIC RESONANCE CHOLANGIOPANCREATICOGRAPHY FOR IMPROVING THE QUALITY OF IMAGES IN LIVING LIVER DONORS

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The evaluation of biliary antomy in living donor liver transplantation (LDLT) is very important and performed most commonly using intraoperative cholangoigraphy. Magnetic resonance cholangiopancreaticography (MRCP) has been increasingly used for evaluations of LDLT donors due to its noninvasiveness. Some authors have used morphine to enhance the image quality of MRCP. The objective of our study is to determine the effectiveness of morphine augmented MRCP for illustrating the biliary anatomy of LDLT donors. We have been using MRCP in LDLT donor evaluation since 2007. We recently changed the protocols of preoperative MRCP with morphine injection. So we divided the donors into two groups between MRCP without morphine and MRCP with morphine. Thirty seven LDLT donors were retrospectively evaluated with preoperative MRCP. The quality of MRCP images was assed by visualization grading score between two groups.

	M(−)	M(+)	p-Value
Number	26	11	N/A
Age	32.19 ± 10.12	28.18 ± 8.91	0.263
Male/Female	20/6	9/2	0.556
Duct type(A1A2A3A4)	19/2/1/4	7/1/1/2	0.709
Operative cholangiogram	18	0	N/A
MRCP score	1.32 ± 0.54	1.81 ± 0.40	0.04
Duct reconstruction(DD/HJ)	17/9	10/1	0.114
Total operative time	454.5 ± 25.76	434.0 ± 29.02	0.186

Biliary anatomy was classified according to the classification proposed by Huang and colleagues. Pre-morphine era group (M−) and Morphine era group (M+) donors were 26 and 11 respectively. The quality of MRCP in M+ group was superior to M− group ($p = 0.04$). Intraoperative cholangiography and biliary exploration revealed that 26 donors (70.3%) had conventional and 11 (29.7%) had aberrant biliary anatomy. Three donors (8.1%) had type A2 biliary anatomy; 2 donors (5.4%), type A3; 6 donors (16.2%), type A4. Preoperative MRCP with morphine represents more improving visualization of the biliary tree than without morphine in LDLT donors. However, it is not result in beneficial effect on clinical outcome.

BO168 NEW TECHNIQUE OF BILIARY RECONSTRUCTION IN LEFT LATERAL SECTION LIVER GRAFT

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Purpose: The problem of biliary complications after left lateral liver section transplantation in kids remains actual. According to the world experience the frequency of biliary complications in the early postoperative period averages 25%.
Method: From January 2013 to February 2015 111 left lateral section transplantations were performed in children aged from 2.7 to 12 months, with a body weight from 3 to 9 kg. The left lateral section grafts were got from living related donors together with the liver round ligament. The hepaticocaval, portal and arterial graft revascularization was performed by standard technique. Biliary reconstruction was routinely performed by Roux-en-Y end-to-sied hepaticojejunostomy, with PDS 5-0 or 6-0 interupted sutures. In 85 patients (76%) only one anastomosis with single bile duct was applied. In other 26 patients (24%) the graft had two or three bile ducts, which were anastomosed in the same manner with the help optic magnification. After finishing end-to-side anastomosis the round ligament of graft was fixed along the upper side of biliodigestive anastomosis and wound surface of liver graft by 2–3 sutures to the gut wall.
Results: In presented cohort biliary fistula occurred only in 3 (3%) patients. The rest 108 (97%) patients had no biliary complications.
Conclusion: According to received results we conclude, that described technique reduces frequency of postoperative biliary fistula in pediatric patients and requires further study.

BO169 LIVING DONOR LIVER TRANSPLANTATION: ONE CENTER EXPERIENCE ON DONOR SAFETY AFTER 90 CONSECUTIVE CASES

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Ospedale Niguarda Ca' Granda

Background: Donor safety must be considered a priority in live liver transplantation (LDLT). The aim of this study is to evaluate the outcome of live liver donors in our center giving special attention to surgical complications and to their treatment.
Material and Methods: Between March 2001 and December 2014, 90 live donors underwent right hepatectomy (5-6-7-8 segments). Median hepatic vein has always been left to the donors. The aim of this study was to analyze donor peri-operative morbidity: surgical outcome of donors and complications were classified according to Clavien classification modified for live liver donors.
Results: No donor died and all the donors are alive after a median follow up of 63.2 ± 12.6 months. Three intraoperative complications are reported. All donors had complete recovery after donation. The overall complication rate was 18% (17 donors out of 90). Seven of these (7.7%) have been classified according to Clavien classification as major complications (grade 2b) but only in two cases donors underwent surgical treatment.Discussion. Donor safety should be considered the first end point for LDLT. Biliary complication seems to be the most frequent, thus the surgical management of the biliary tree should be improved during the resection and after the procurement. Despite results reported in some series from western countries, the overall complication rates in our experience appeared significantly lower than other. On the other hand, huge difference remains comparing the western series to the Asian series, and this is explicable by the number of cases performed. However, there is not a register for living liver donors in western countries. Therefore, results difficult to understand the real impact of donor safety in this area.

009 ETHICS/LAW/PSYCHOSOCIAL/PUBLIC POLICY

BO171 LIVING DONOR KIDNEY TRANSPLANTATION NEEDS A DIFFERENT ETHICAL FRAMEWORK

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There is a persistent shortage of organs for kidney transplantation. General consensus remains that living donation (LD) should only be used as an alternative to deceased donation (DD). Attempts to increase DD have resulted in decreased organ quality, translating into reduced survival and more rapid return to dialysis. LD provides high quality grafts and the potential to eliminate organ shortage. The question is whether it is ethical to preferentially offer DD when LD is a superior therapy.

More than 80 000 patients are on the kidney transplant waitlist, with 30 000 new patients added annually and a median wait time of 3–4 years. Deceased donation has remained at 6000/year for the past 10 years. 40% of recipients receiving DD are dialysis-dependent after 10 years, with an allograft half- life of 8.8 years. In comparison, 20% of LD recipients were dialysis-dependent after 10 years, with an allograft half- life of 12 years. Two-year mortality of living donors is 0.03–0.05%. There is no demonstrated increased risk of ESRD in living donors in comparison to the general population.

In view of these facts the focus of the ethical discussion about LD needs to be shifted from the donor to the recipient. LD offers a large, potential source of quality allografts, shortens waitlist times, and improves long-term outcomes. LD should be openly promoted, and a well- delineated donor informed consent is necessary to fulfill the ethical imperative of donor autonomy and surgeon moral agency.

BO172 LIVER TRANSPLANTATION AND FACEBOOK

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Introduction: Facebook (FB) allows for the formation of groups of people with similar interests who can interact in various ways. We examined a new use of the FB network for patients undergoing liver transplantation (LT).
Patients and Methods: In November 2013, a FB group named "1000 liver transplants at the Policlinico Hospital of Milan" was created. All patients who had undergone LT at our center were invited to join the group. The aim of this study was to assess the psychological impact of interactions between neo-transplanted patients with more experienced long-term survivors. In September 2014 we examined the age, sex, and the number of transplanted or not transplanted members. With a psychologist, we then evaluated the comments made in the FB Group and their psychological aspects.
Results: From June 1983 to September 2014, 1037 LTs were performed in 928 patients. In September 2014, 629 (67.7%) of those patients were still alive (222 females and 407 males), and 139 patients (22%) joined our FB group. Of the patients who joined our FB group, 57 were females and 82 were males, corresponding to 25.7% and 20.1% of the living females and males, respectively (p = NS). Members of the FB group were younger (50 $\pm$ 15 year) than non-users (53 $\pm$ 15 year) ($p = 0.03$). The FB group is presently composed of more than 400 members. In March 2014, the success of the FB Group led us to have a public meeting to celebrate the 1000 liver transplants at our hospital. A new event to spread the culture of organ donation is currently being organized with the FB Group users, doctors and head officers of public health institutions.
Conclusion: This is the first report of a FB Group for liver transplanted patients. This study shows that a FB group for liver transplanted patients provides a strong emotional impact. The educational aspect of this type of group on transplanted patients and on patients in waiting list, and the effects on the culture of organ donation seem to deserve attention.

BO173 THE CRIMINAL PATIENT? A SYSTEMATIC REVIEW ON PATIENTS' INVOLVEMENT IN THE HUMAN ORGAN TRADE

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Background: In 2012 the European Commission awarded 'The HOTT Project': an international research project against trafficking in human beings for the purpose of organ removal (THBOR). This project aims to generate more knowledge and awareness about this crime. The project's first report, a large literature review, fulfils this objective by describing existing information on the incidence and nature of THBOR, in particular the persons involved. Our sub-study focused on the role of recipients. By conducting a systematic literature review we aimed to identify the nature and extent of patients' involvement in a) travel for transplantation, b) commercial transplantations and c) THBOR.
Methods: We searched Embase, Medline, Web of Science, Scopus, PubMed, Cochrane and Google Scholar. The methodology and results of this systematic literature review are in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. All English studies published in full text after 1 January 2000 were included. Presentations, abstracts, opinion papers, non-English records and publications lacking methodology were excluded.
Results: The search yielded eighty-five records. Of these, seventy-six records present patients who travel. Patients travel worldwide for transplantation of hearts, lungs, livers, and most commonly, kidneys. The most common destination countries are India, China and Pakistan. 51 records describe these patients as 'transplant tourists'. 17 records state that patients bought organs domestically. Only few present the amount and the beneficiary. Patients make payments to "donors", brokers, hospitals, unidentified "companies" and doctors. The most common form of organ purchase is through a "transplant package". Three studies mention the involvement of patients in the exploitation of their donors.
Conclusion: Although it is likely that patients who travel for transplantation purchase organs on the black market, the literature provides only.

BO174 INTEGRATING MENTAL AND PHYSICAL HEALTHCARE IN LONG-TERM KIDNEY TRANSPLANT RECIPIENTS

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Background: In the UK integrating physical and mental healthcare is a key national priority. IMPARTS (Integrating Mental & Physical healthcare in Research Training & Service) is a package developed to facilitate integration through the collection of patient reported data via tablets and offering guidance on referral pathways. An increased prevalence of psychological illness, in particular anxiety and depression, in long-term kidney transplant patients (LKT) has been documented and is associated with increased morbidity.
Methods: Using the IMPARTS package we screened 99% (n = 299) of LKT attending between 07/2013 and 11/2014. Measures included: depression (Patient Health Questionnaire PHQ-9), anxiety (Generalised Anxiety Disorder Assessment GAD-7), medication adherence, and functional impairment scores.
Results: The mean age of LKT screened was 53.0 years. 36.8% were female. We identified probable Major Depressive Disorder in 4% (11/299) and probable Generalised Anxiety Disorder in 5% (16/299) of LKT screened. Patients with mood difficulties or significant worry were referred to the team clinical psychologist for further assessment. Medication Adherence data showed 39.2% forget to take medication; 8.2% intentionally do not take medication.

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

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

BO175 ENHANCING BENEFICENCE AND JUSTICE IN LIVING DONOR ORGAN TRANSPLANTATION: LIFELONG MEDICAL COVERAGE FOR LIVING DONOR

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Baylor University Medical Center

Living kidney donation allows the expansion of the donor pool to allocate kidneys to an additional 6000 recipients/year. This altruistic act releases thousands of patients from dialysis, and makes available thousands of organs from deceased donors to patients that do not have a living donor. In light of the alleviation of multiple financial, physical and emotional burdens their donation provides, long-term donor health should be of the highest priority. The majority of publications have revolved around the issue of donor safety, while consistent long -term follow-up for living donors is still lacking.

While the OPTN only requires 2 years of data after donation, this timeframe is insufficient, since some of the effects of donation may not be apparent for at least a decade. At this time, there is no clear incentive for donors to adhere to a 2-year follow-up, or beyond, hindering preventive care that may have recognized and avoided end -stage renal disease among other health conditions. Long -term donor health care coverage should be addressed, not for financial gain, but for day–to-day needs and permit donors with financial constraints or life contingencies to fulfill donation. Offering lifelong medical coverage for donors has many significant advantages, which allow for increased donation without fear of financial repercussions, restraints, or delay in medical care.

Table 1 Advantages of offering donor lifelong medical coverage

1. Ability to offer preventive interventions with follow -up and insurance coverage
2. Expand living donation to individuals who otherwise would be reluctant to donate for financial reasons, or lack of insurance
3. Ensure compliance with follow -up regimen
4. May reduce number of donors who progress to end -stage renal disease if not cared for
5. Reduce medical and social financial burden
6. Provide long -term donor follow -up data to optimize future candidate selection, and minimize post nephrectomy medical issues

Offering lifelong medical coverage to living donors provides a stronger ethical foundation to the practice of living donor transplantation: delivering optimal medical care, providing long-term clinical data to allow for better and safer donor selection, and providing tangible compensation to the donors. Long-term medical coverage is medically indicated, financially savvy, and above all ethically obligatory.

BO176 TRAJECTORIES OF ANXIETY AND DEPRESSION OF LIVER TRANSPLANT CANDIDATES DURING THE WAITLIST PERIOD

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Background: Although anxiety and depression are common among liver transplant candidates, little is known about the evolution of anxiety and depression during the waitlist period. The aim of this study was to explore trajectories of anxiety and depression of liver transplant candidates during the waitlist period and to gain insight into demographic, clinical and individual variables associated with these trajectories.
Methods/Materials: A longitudinal study among 216 liver transplant candidates was performed, in which participants filled out a questionnaire with measures regarding anxiety, depression, demographic and individual variables. Measures regarding anxiety and depression were repeated every 6 months until transplantation, removal from waiting list, or end of study. Clinical variables were retrieved from the medical record. Latent class analyses was used to identify distinct trajectories. Multinomial regression analyses were used to explore variables associated with the distinct trajectories.
Results: Three trajectories regarding anxiety were identified: below clinical level (50%), slightly above clinical level (32%), and high above clinical level (18%). Regarding depression four trajectories were identified: below clinical level (28%) slightly below clinical level (42%), slightly above clinical level (25%), and high above clinical level (5%). All trajectories were consistent over time. Experiencing more liver disease symptoms, a lower level of mastery, and the use of emotional coping were significantly associated with higher symptom levels on the trajectories of anxiety as well as the trajectories of depression.
Conclusion: Given the persistent nature of symptoms of anxiety and depression during the waitlist period, it is important to screen liver transplant candidates for psychological problems early in the transplant process. Consequently appropriate interventions can be undertaken to optimize the psychological health of the transplant candidate.

BO177 SHOULD ADOLESCENTS AND YOUNG ADULTS QUALIFY AS LIVING KIDNEY DONOR CANDIDATES? A QUALITATIVE INTERVIEW STUDY WITH TRANSPLANT PROFESSIONALS

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Background: Although living kidney donation (LKD) has become an increasingly common procedure, European and U.S. transplant centres disagree as to whether adolescents (12–17 years) and young adults (18–25 years) should qualify as donor candidates. As the viewpoints of professionals may contribute to a better understanding of the ethical arguments underlying this disagreement, we aimed at exploring transplant professionals' attitudes towards LKD by minors and young adults.
Methods: We conducted fourteen in-depth interviews with a purposive sample of international transplant professionals from various professional backgrounds. Our grounded theory method for analysis was guided by QUAGOL, a systematic approach based on the constant-comparative method.
Results: Professionals characterized their attitude as being careful, as some ethical concerns about LKD were deemed more relevant for young individuals. Specifically, they worried about the uncertain long-term medical and psychosocial risks of LKD, especially to an older recipient. They also worried about donors' capacity to consent, which is more likely to be affected by their developmental stage (insufficient understanding, impulsivity, unstable values, feelings of obligation) or family pressure. Concerns were more pronounced for LKD to unspecified recipients or parents, whereas professionals were more supportive if the recipient was a close sibling or the donor's own child. Nevertheless, most professionals supported an age limit of eighteen years, due to difficulties in evaluating maturity on a case-by-case basis.
Conclusion: Our findings suggest that professionals' degree of concern about the decision-making and long-term impact of LKD depends on the legal age of maturity, as well as the strengt of the donor-recipient relationship. More research on the long-term medical and psychological outcomes in young adult donors is likely to shed more light on the acceptability of LKD by adolescents and young adults.

BO178 THE B-SERIOUS SYSTEMATIC REVIEW AND META-ANALYSIS ON CORRELATES AND CONSEQUENCES OF ALCOHOL USE AFTER SOLID ORGAN TRANSPLANTATION

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Background: Reviews on alcohol use in transplantation (Tx) mainly focus on alcoholic liver disease and risk of relapse post-Tx, and do not provide insight on alcohol use in heart, lung or kidney Tx. Hence, this systematic review with meta-analysis aims to synthesize the evidence on correlates and outcomes of any alcohol use after heart, lung, kidney and liver Tx (PROSPERO protocol CRD42015003333).
Methods/Materials: We searched PubMed, Embase, PsycINFO, and CINAHL through July 1, 2012 for 1) quantitative studies, 2) in adult heart, liver, kidney and lung Tx, and 3) on associations between post-Tx alcohol use and correlates and/or clinical, economic or quality of life outcomes. Title/abstract and full text evaluation, data extraction and quality assessment were done by 2 reviewers independently. A pooled odds ratio (OR) with 95% confidence interval was computed for each correlate/outcome investigated independently 5 or more times.
Results: Fifty-nine of 3324 papers were included (95% liver Tx; 53% from USA; mean sample size 138; 72% male; mean age 48 years; median time post-Tx 65 months). Post-Tx alcohol use was on average 24% (range 5.5–52.8%). Of 88 correlates studied, a pooled OR was computed for 18, of which 11 were significantly associated with a higher odds of post-Tx alcohol use: post-Tx employment, being single, poor social support, smoking pre- or post-Tx, history of illicit drug use, pre-Tx sobriety <6 months, first degree relatives with alcohol-related problems, history of psychiatric illness, pre-Tx treatment for alcohol-related problems, and higher scores on pre-Tx risk prediction scales. Moreover, post-Tx alcohol use was significantly associated with a lower odds of late acute rejection and higher odds of developing a fatty liver.
Conclusion: This systematic review with meta-analysis yielded unique insights on correlates and outcomes of any alcohol use highlighting important avenues for both future research and improved clinical care for all Tx pati.

BO179 INTERNATIONAL INITIATIVE TO ENHANCE THE ORGAN DONATION AND TRANSPLANTATION SYSTEMS IN THE BLACK SEA AREA: THE BSA PROJECT

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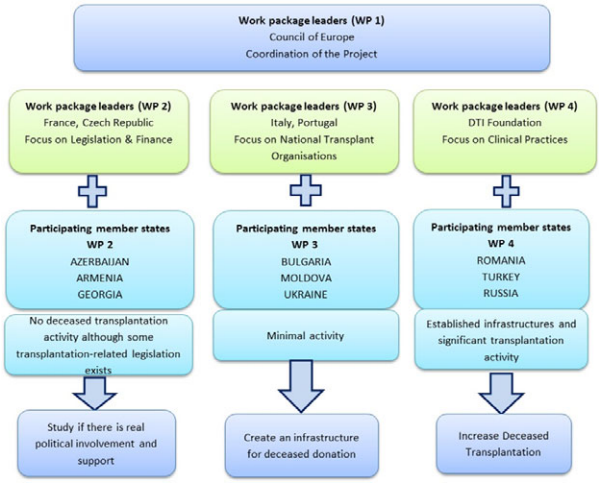
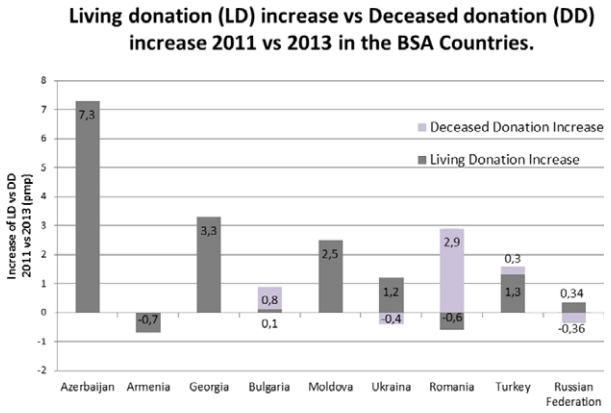
Background: The Council of Europe(CoE) launched in 2011 a 3 year collaboration project that aimed to battle organ shortage and improve the access to transplant health services in the Council of Europe BSA member states (Armenia, Azerbaijan, Bulgaria, Georgia, Moldova, Rumania, Russian Federation, Turkey and Ukraine) through the development of safe and ethical Donation and Transplantation (D&T) programmes.
Objective: To support the development of D&T programmes through close inter-state cooperation between national health organisations and relevant stakeholders.
Methodology: Focused in the level of development of D&T in each Black Sea Area (BSA) member state, the following working packages (WP) were established: a)WP1: Coordination of the Project (CoE), b)WP2: Development and implementation of an effective legislative and financial framework (Czech Republic and France), c)WP3: Establishment of National Transplant Authorities (Italy and Portugal), d)W4 Clinical Practices (Spain and DTI Foundation).



Data collection, surveys and experts visits were performed to get first-hand information in each participant country at national, regional and hospital level by detecting problems and proposing solutions.
Results: Data analysis showed a positive impact of the project represented by a tendency to raise the D&T rates in all the countries.



Conclusions: The increase of the donation rates is a result of an implementation of legislative, organizational and institutional recommendations performed by the CoE, the efforts of the Ministry of Health (MOH) of each country and synergies with other European projects placed in the BSA area. BSA project made possible to analyse, assess and compare the different legal and organizational systems of the BSA countries. As a consequence of the outcomes, BSA countries should invest themselves in the implementation of the recommendations resulting from this project in order to achieve their organ donation.

BO180 A SYSTEMATIC TRANSLATION PROCESS FOR CROSS-CULTURAL ADAPTATION OF THE INSTRUMENT: ATTITUDES TOWARDS ORGAN DONOR ADVOCACY SCALE (ATODAS)

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Specific behavior among intensive care unit (ICU)-staff is significantly associated with if there's consent to, or decline of organ donation. In 2011, Flodén et al. developed the instrument "Attitudes towards organ donor advocacy scale" (ATODAS) which measure the attitudes toward organ donor advocacy among intensive and critical care nurses. The cross-cultural adaptation process is necessary to effectively use existing instruments in other cultural and language settings. Using a multi-step approach is considered as best practice.

The aim of this study is to translate the ATODAS instrument (questionnaire) into an international context and to ensure the content validity of the ATODAS instrument, "American version".
Methods: Our cross-cultural adaptation process was guided by Brislin's back-translation approach and guided by the conceptual framework of Polit and Beck to ensure semantic equivalence. Content validity was validated with reference to Lynn's criteria. The multi-step approach included five steps:

1. Initial translation by a licensed interpreter.
2. Back-translation by a different interpreter.
3. Synthesis of these translations by an international group of experts.
4. Expert committee by seven designated nurses in Los Angeles.
5. The 56 item instrument was reduced to 51 items.
6. Test and re-test of the pre-final version with ICU nurses at two hospitals in Los Angeles.

Results and Conclusions: Undertaking this multi-step approach has effectively ensured that the cross-cultural adaptation process resulted in a stronger instrument. Our translated and tested instrument was adapted to be culturally relevant in order to yield more reliable and valid results for use in a larger research study, to measure organ donor advocacy among American intensive and critical care nurses. Our American version of the ATODAS instrument will provide a clear framework for other researchers choosing to utilize our instrument for work in other cultural, geographic, and population settings.

BO181 URINARY CATHETER CARE FOLLOWING RENAL TRANSPLANTATION: HOW SOON CAN IT SAFELY BE REMOVED? OUTCOMES OF A UK-WIDE NATIONAL SURVEY OF RENAL TRANSPLANT SURGEONS AND SINGLE-CENTRE EXPERIENCE

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Background: There is no consensus on duration of urinary catheterisation (UC) following renal transplant (RTx) surgery. Current duration of UC appears to vary throughout UK transplant centres from post-operative day-2 to day-7. This study describes outcomes of a national survey dispatched to UK renal transplant surgeons regarding post-operative urinary catheter care (POUCC). We also investigated our units current POUCC practice (UC removal day-2) and subsequent outcomes.
Methods: 1) A survey study was designed to explore various contributing factors influencing decision making towards POUCC amongst consultant RTx surgeons. The national online survey was distributed to all UK renal transplant consultants. Opinions were sought with regards to current POUCC in live donor recipients, DCD and DBD renal transplants.

2) Retrospective RTx-data was collected from 2010 to 11. Outcomes analysed included length of hospital stay, urinary leak, haematuria, urinary obstruction, re-catheterisation and urinary-tract infecion within 30 days of RTx. Exclusion criteria: anuric, on a second or subsequent RTx, who underwent ureteric anastomosis into systems other than the urinary bladder and who underwent follow-up of <1 year post RTx. SPSS 21 was used for analysis, where $p < 0.05$ was considered significant.
Results: 1) Individual response rate was 50% (47 respondents), representing 83% of UK transplant centres. Results from the national survey are summarised below (tables 1,2,3 and 4):

Table 1

Variable:	% Responders who would consider this acceptable (post-operative day): Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Live recipient catheter removal	0%	7%	2%	13%	78%	0%	0%
DBD recipient catheter removal	0%	6%	4%	13%	77%	0%	0%
DCD recipient removal	0%	6%	4%	13%	75%	0%	2%
Native urine output: Preferred duration of catheterisation	0%	18%	6%	6%	47%	6%	17%
Earliest catheter removal IRRESPECTIVE of urine output	0%	15%	26%	34%	25%	0%	0%

Table 2

Variable:	% Responders who said yes	% Responders who said no
Does recipient native urine output influence duration of postoperative catheristaion?	17%	83%
Post-renal transplant: Patient CAN be discharged with indwelling catheter?	98%	2%

Table 3

Reason(s) for prolonging catheterisation:	% Response
To prevent urinary leak from neo-uterovesical anastomosis	64%
To use catheter for irrigation (haematuria)	23%
For patient convenience	51%
For accurate measurement of fluid balance / Urine output	36%

Table 4

Variable:	Strongly agree	Agree	Impartial	Disagree	strongly Disagree
Length of hospital stay unecessarily prolonged in patients with an indwelling UC? (% Response)	11%	17%	17%	42%	13%

The majority of UK transplant units (77%) remove UC on day-5. Recipients native urine output and prevention of urinary leak were significant influential factors ($p < 0.026$, $p < 0.044$ respectively) with regards to urinary catheter duration and purpose.

2) In our analysis, there were 161 RTx fulfilling our criteria. The male: female ratio was 2:1, with a mean age (± SD) of 50.1 years (± 13.1). Outcomes from our single-centre are shown below (table 5):

Table 5

Variable:	Urinary catheter removed day 2 ($n = 117$)	Urinary catheter removed >2 days ($n = 44$)	Significance (p-value)
Length of hospital stay (mean ± SD)	4.5 (± 0.4) days	8.4 (± 3.6) days	0.002
Urinary Leak	4	1	0.711
Haematuria	5	1	0.559
Urinary obstruction / Re-catheterisation	5	2	0.939
Urinary tract infection (UTI)	5	5	0.049

Conclusion: There are no internationally agreed criteria regarding duration of post-operative UC following RTx. This study suggests national opinion regarding UC removal should be sooner (26% post-operative day-3 and 34% day-4) than current national practice (day-5). However, outcomes from our single centre study suggests UC removal on day-2 post RTx is safe practice, with no significant detrimental sequelae when compared to those who underwent UC removal after 2 days. Patient length of stay is significantly reduced with UC removal on day-2. Further studies are required to evaluate.

BO182 IMPACT OF DISTANCE FROM TRANSPLANT UNIT ON OUTCOMES FOLLOWING KIDNEY TRANSPLANTATION

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Cardiff Transplant Unit

Introduction: Cardiff Transplant Unit is the only transplant centre in Wales serving a population of 2.3 million and a geographical area over 14 000 square kilometres. Following transplantation, many patients travel long distances for follow-up care. Many studies have examined the influence of distance from transplant centre on access to transplantation, but few have examined post-transplant outcomes.

Methods: The online 'AA Route planner' was used to determine distance from transplant centre for all kidney transplant recipients transplanted between April 2009 and March 2014. Outcomes measured were rates of acute rejection and graft survival.

Results: Over a 5-year period, 585 kidney transplants were performed, of which 570 were followed up for a median 35 months. 386 (67.6%) were male. Median age was 54 years (range 15 – 80). 190 (33.3%), 176 (30.3%) and 205 (36.4%) were living donor, DBD, and DCD kidney transplants respectively. 98 (17.2%) patients lived within the catchment area of the local health board of the transplant centre. Median distance from home to transplant centre was 33.7 km (range 1.3 – 257.4 km). 131(23.1%) patients experienced at least one episode of rejection within the follow-up period. Mean distance for those with and without a rejection episode was 44.4 km and 49.5 km respectively ($p = 0.769$). The rejection rate in the nearest and farthest distance quartiles was 28% and 20% respectively ($p = 0.12$). One-year graft survival for nearest and farthest quartiles was 99% and 97% respectively and 5-year graft survival was 79% and 89% respectively (log rank p-value of 0.31). Mean distance for those with and without graft failure was 48.9 km and 48.3 km respectively ($p = 0.149$).

Conclusion: This study has demonstrated that distance from transplant centre does not affect outcomes following kidney transplantation. The centralised practice which involves a low threshold for rapid assessment and readmission of patients post-transplantation appears to be safe.

BO183 EVALUATION OF MDRD4, CKD-EPI AND MODIFIED COCKCROFT-GAULT EQUATIONS TO ESTIMATE GLOMERULAR FILTRATION RATE IN THE ELDERLY RENAL TRANSPLANTED RECIPIENTS

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Background: The use of equations to estimate glomerular filtration rate (eGFR), in the elderly renal-transplanted (≥60 years at RTx) recipients, has never been performed. Because age, body weight and serum creatinine are variables of these equations, developed in a younger CKD cohort, they may not adequately estimate mGFR in the elderly population.

Methods: Data from all mGFR, by plasma EDTA-Cr51 clearances (EDTA-Cr51Cl) ($n = 451$), in 327 RTx patients from Jan/2008 to Sep/2014 were divided in 2 groups: Elderly group (EG $n = 70$): 65 ± 4 years, 111 EDTA-Cr51Cl, and Younger group (YG $n = 257$): 42 ± 11y, 340 EDTA-Cr51Cl. The results were compared with the Cockcroft-Gault corrected by body surface area (CG-BSA), the MDRD4 and the CKD-EPI equations, using parameters at each EDTA-Cr51Cl. Results

Besides the mean age, EG were under mTOR more frequently than the YG. Height, body weight and BSA did not differ. mGFR was measured at 8 ± 11 vs. 15 ± 16mo after RTx in the EG and YG, respectively ($p = 0.002$). Mean mGFR was lower in the EG than in the YG (46 ± 15 vs. 54 ± 20 ml/min/1.73 m^2, $p = 0.019$). In the YG, (validation set) our results confirmed data showing the MDRD4 is the most appropriate eGFR (bias0 ± 13 ml/min/1.73 m^2 and 30%, 10% accuracy of 90%, 71% respectively. In the EG, mean mGFR (46 ± 15 ml/min/1.73 m^2) was not significantly different from CKD-EPI, C-G BSA and

MDRD4 (47 ± 17 vs. 45 ± 15 vs. 47 ± 17 ml/min/1.73 m^2, respectively). The CG-BSA equation had a statistically lower bias than the MDRD-4 and CKD-EPI (0 ± 13 vs. 2 ± 11 vs. 1 ± 12 ml/min/1.73 m^2, respectively, $p < 0.025$) with similar 30%, 10% accuracy of 83%, 66%. Because 80% ($n = 89$) of the EG had mGFR≤60 ml/min/1.73 m^2, another analysis was conducted in this range. All equations presented a similar bias (~2 ± 11 ml/min/1.73 m^2 with similar 30%, 10% accuracy of 80%, 60%, respectively.

Conclusion: The CG-BSA equation is a valuable tool to monitor GFR in the elderly RTx recipients for all ranges of mGFR. For mGFR ≤60 ml/min all available equations showed similar bias and accuracy.

007 DONATION/RETRIEVAL

BO184*

KIDNEYS FROM DONORS WITH ACUTE KIDNEY INJURY (AKI): FRIEND OR FOE?

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Background: The widening gap between supply and demand in kidney transplantation (ktx) has lead to increased use of kidneys from marginal donors. Despite the organ shortage, donor kidneys with AKI are often declined or discarded. To determine if this policy is justified we have analysed outcomes of AKI in a large UK cohort.
Methods: A retrospective analysis of the UK tx registry evaluated adult deceased donors between 2003 and 2013. Donors were classified as no AKI, or AKI stage 1, 2 or 3 according to AKIN criteria defined by change in creatinine between admission and donation. Relationship of AKI with DGF/PNF, eGFR and graft survival (GS) at 90d and 1y was investigated using risk adjusted Cox regression analysis.
Results: 11 244 kidneys were included in the study. 5% of AKI kidneys were not accepted or transplanted. There is evidence that the chance of graft failure (GF) at 1y is greater for donors with AKI than for those without (GS 89% vs. 91%, $p = 0.02$; OR 1.20 (95% CI: 1.03–1.41)). The odds of DGF and PNF increase with donor AKI stage ($p < 0.005$, $p = 0.04$ resp). Analysis of association between donor AKI and recipient eGFR suggests risk of inferior eGFR with increasing AKI stage versus no AKI ($p < 0.005$; OR 1.25 (95% CI: 1.08–1.31)).
Discussion: This study shows that a significant number of donor kidneys with AKI is discarded. We report a small but significant reduction of 2% in 1y GS of kidneys from donors with AKI. The 20% increased chance of GF due to AKI matches the 17% risk of GF after dialysis treatment for 6 m when compared to pre-emptive ktx, and is significantly lower than the 37% and 55% increased risk of GF when dialysing for longer than 1 or 2 years prior to ktx [Meier-Kriesche, KI 2000]. In this analysis, 1667 recipients received a donor kidney with AKI and still had a functioning graft at 1 year. We conclude that donor kidneys with AKI stage 1 or 2 should not be discarded as they give comparable outcomes; caution is advised for AKI stage 3 donors.

023 KIDNEY

BO185 ECHOCARDIOGRAPHY AND CARDIOVASCULAR RISK: WHAT'S THE RELATIONSHIP IN THE RENAL TRANSPLANT RECIPIENT?

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Introduction: Cardiovascular (CV) disease is the major cause of death among renal transplant recipients (RTR). Unlike end stage renal disease, it is unknown whether echocardiographic abnormalities are useful to identify RTR with high cardiovascular and risk of death.
Objectives: To characterize the metabolic profile, risk of major adverse cardiac events (MACE) and death in a population of RTR. Characterize cardiac function and morphology. Determine which echocardiographic abnormalities predict the risk of MACE and death.
Methods: Retrospective review of 107 RTR in follow-up at our institution, with a functioning and stable graft for longer than 12 months and an echocardiography performed in the last year. Risk of MACE and death using a CV risk calculator specific for RTR and echocardiographic parameters were analysed.
Results: Among 107 patients followed at our institution (57.9% males, 50.4 ± 13.9 years old), 7-years risk for MACE was >10% in 30.9% of patients and 7-years risk for death >10% in 56.1%. Left ventricular hypertrophy (LVH) was present in 55.1%, diastolic dysfunction in 39.3%, dilated left atrium (LA) in 53.3%, high pulmonary artery systolic pressure (PASP) in 29.0%, valvular calcifications in 22.4% and moderate to severe mitral regurgitation (MR) in 3.7%. Mean Ejection fraction was 68.36 ± 6.87%. Univariate analysis showed an increased risk of MACE in patients with LVH [6.9% vs. 14.5% (p 10% and valvular calcifications [OR 3.499 (1.115–10.982, p = 0.032)] and elevated PASP [OR 7.954 (2.412–26.238, p = 0.001)]. Risk for death>10% in multivariate analysis had an independent association with diastolic dysfunction [OR 3.909 (1.261–12.115, p = 0.018)] and with elevated PASP [OR 4.319 (1.201–15.535, p = 0.025)].
Conclusion: Echocardiographic abnormalities identify RTR at increased risk of MACE and death. Valvular calcifications and elevated PASP are significant predictors of MACE whereas Diastolic dysfunction and elevated PASP are significant predictors of death.

BO186 MORTALITY WITHIN THE FIRST MONTH AFTER KIDNEY TRANSPLANTATION – AN OBSERVATIONAL, COHORT STUDY

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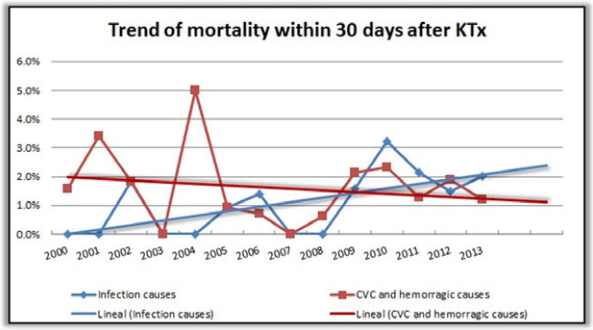
Infection was the principal cause of death after the first year of kidney transplantation (KTx), but the cause of early mortality, was not well described in the actually.

We performed a retrospective, unicentric analysis of mortality in the first 30 days after KTx during January 2000 to May 2014. Older patients than 18 years who received single or combined organ transplantation (COT) from deceased or living donors were included. Data were obtained from medical records and necropsy evaluation. Variables analyzed were age, sex, race, ERSD etiologies, time in dialysis, BMI, living or deceased donor, induction therapy and COT. Statistical analysis was done by Mann-Whitney test, Chi-sq test and Step-wise logistic regression.

In this period, a total of 2390 patients were transplanted in our center. Mortality within the first 30 days after KTx occurred in 87 patients(3.5%), majority of them, were male(60%), white (59%), mean age was 53 ± 12 years and a mean time of dialysis were 52 months. The principal ERSD etiologies were DM (29%), Hypertension (24%) and Glomerulonephritis(22%) and high percentage was transplanted with deceased donors (92%). The most frequent cause of death was infection with 31 cases (36%) followed by cardiovascular (23%), hemorrhagic (21%) and other causes (20%). We observed a raising trend increase of death by infection causes (DIC) during the period analyzed Chi-*sq* 9.09, p = 0.003, as opposed to cardiovascular and hemorrhagic causes, that's tended to reduce. Patients with DIC more frequently dead after the 7*th* day of hospitalization (73% p = 0.006), were more often COT patients (58% p = 0.06) and had less dialysis time before KTx(*P* = 0.07), when compared with other causes of dead. In multivariate analysis the differences between DIC and others death causes were COT p = 0.02 OR4.63 and death after 7*th* day of KTx p = 0.002 OR0.18.

Death by infectious diseases took a longer time to be set as a principal cause of mortality and were associated to more complexity surgery, as COT.



BO187 TRANSPLANTING THOSE WAITING THE LONGEST

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Introduction: Transplantation is the optimal form of renal replacement therapy for suitable patients with end stage renal disease. Long term outcomes improve when the time spent on dialysis is minimised, and individuals with prolonged waiting times can become unfit for transplantation. Those with pre-existing HLA antibodies often wait a disproportionately long time.
Methods: All patients in Northern Ireland (NI) active on the UK deceased donor renal transplant waiting list on 1 Jan 2013 were ranked according to waiting time. All waiting longer than 5 years were identified and those that were very highly sensitised reviewed. Antibodies that were currently not detectable or present at low titres were removed from the unacceptable antigens listed with NHS Blood and Transplant.
Results: There were 30 patients waiting longer than 5 years. The mean waiting time for transplantation was 8 years 5 months, (range 5 years. 1 month – 21 years. 3 months) and mean panel reactive antibody sensitisation was 71%, (range 0 – 100%); 16 (53%) were very highly sensitised (>95% antibodies). The registered unacceptable antigens were altered in 10 (33%).Within 24 months, there were 30 transplants in 28 (93%) patients, one is now unfit for transplantation and one is currently suspended. 8 (27%) were from living donors. Alemtuzumab was given in 9 transplants and Rituximab in 2. The 12 month graft survival was 87%. Of the 4 grafts that failed: 2 had primary non-function due to donor characteristics, 1 failed due to non-recovery of recurrent episodes of AKI after 5 months, and 1 failed at 10 months due to recurrent anti-GBM disease. Two of these patients have seen been transplanted successfully. 12 month patient survival was 100%. In NI there are currently only 2 patients waiting longer than 5 years.
Conclusion: A proactive approach to highly sensitised patients can enhance the opportunities for transplant and should be considered for those with high HLA antibody levels before they have a prolonged duration on dialysis.

BO188 COMPARABLE TRANSPLANT OUTCOMES BETWEEN DBD AND DCD KIDNEY GRAFTS UP TO 5 YEARS POST-TRANSPLANT: SINGLE CENTRE EXPERIENCE

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Introduction: This study aimed to determine the most recent results of kidney transplantation (KT) from donation after brain death (DBD) and circulatory death (DCD). Primary endpoints were graft and patient survival, and graft function. Acute rejection and post-operative complications were assessed as secondary endpoints.
Patient and Methods: This retrospective mono-center review consisted of 226 DBD- and 104 DCD-KT between 2008 and 2014.
Results: Graft survival was comparable between two groups (95.1 vs. 91.1% at 1 year, 92.8 vs. 91.1% at 3 years and 89.2 vs. 91.1% at 5 years). 46% and 40% of graft loss were attributed to patient death with a functioning graft and rejection. Patient survival was comparable between 2 groups (97.8 vs. 95.1% at 1 year, 94.1 vs. 91.2% at 3 years, and 89.6 vs. 82.3% at five years). Etiology of patient death included cardiac arrest (16.7%), infection (16.7%), cancer (13.3%), and unknown cause (46.7%). Delayed graft function occurred in 14.6% of DBD- and 30.8% of DCD-KT (p = 0.001). Primary non function was encountered in 2.6% DBD- and 4.8% DCD-KT (p = ns). Graft function was worse in DCD than DBD up to 3 months post-transplant (p = 0.034), however, no difference existed afterwards. Biopsy-proven acute rejection was found in 12.8% and 13.5% of DBD- and DCD-KT during an average 3 months post-transplant (p = ns). This rate was 7.1% vs. 8.9% on surveillance biopsy performed between 3 and 6 months post-transplant (p = ns). Post-operative

complication rate was comparable between 2 groups, concerning patient death, reoperation, transfusion, perirenal hematoma, macroscopic hematuria, urinary obstruction, wound problem, and infection. Nevertheless, contamination of preservation solution occurred more commonly in DCD than DBD (0.4% vs. 3.8%, p = 0.036).
Conclusions: Despite worse early graft function, DCD-KT was not inferior to that originating from DBD up to 5 years post-transplant, therefore deserves to be used.

BO189 EARLY PLASMA-CREATININE CHANGES PREDICT ONE-YEAR GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: Validated surrogate endpoints for long term kidney graft function are needed in clinical kidney transplantation trials. This study evaluates the association between initial kidney graft recovery and graft function 1 year posttransplant.
Methods: A single centre, observational, cohort study including 100 kidney transplants followed 1 year at Aarhus University Hospital. All p-creatinine (p-cr) values at time of transplantation and 30 days posttransplant were registered along with relevant patient characteristics. In case of temporary dialysis posttransplant, p-cr was gathered until 30 days after the last dialysis. One-year p-cr and graft outcome were registered and in case of death or graft loss, patients were excluded from the analysis ($n = 4$). The observed, time dependent changes in p-cr were modulated for each, individual patient by an exponential, logistic, or a linear model, and the time to a 50% decrease in p-cr was estimated. eGFR 1 year posttransplant was calculated using the simplified Modification of Diet in Renal Disease (MDRD) formula. A multiple linear regression model was used to analyse the association between the time to a 50% drop in p-cr and eGFR after 1 year.
Results: The time to a 50% drop in p-cr correlated negatively with eGFR at 1 year ($n = 96$, $r = -0.375$, beta $= -0.112$, p = 0.0002). The correlation persisted when corrected for donor type, recipient age, gender, initial p-creatinine level, and cold ischemia time ($n = 90$, p = 0.018). A positive correlation between the time to a 50% drop in p-cr and the total days of hospitalisation 30 and 365 days posttransplant, as well as the number of performed ultrasounds and kidney biopsies 90 days posttransplant, was also found.
Conclusion: Early graft function differences may be important for long-term outcome. Time to a 50% drop in p-cr might be used as a surrogate marker in renal transplant studies, and includes both patients with or without temporary posttransplant dialysis need.

BO190 PATIENT-RELATED FACTORS AFFECTING THE INITIAL TACROLIMUS TROUGH LEVEL AFTER KIDNEY TRANSPLANTATION

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Background: In general, the recommended tacrolimus (Tc) initial dose is calculated per kg of body weight and fixed at 0.1 mg/kg/dose BID. Some observations suggest that in selected groups of patients such dosing may result in Tc tocixity in the early posttransplant period. The aim of our study was to find the factors increasing an initial Tc trough level.
Methods: We performed the retrospective analysis (2000–2013) of 468 consecutive kidney transplant recipients initially treated with immunosuppressive regimen containing tacrolimus BID, mycophenolate, and steroids. The analysis included the first assessment of Tc trough levels and patient-related factors that might affect the pharmacokinetics of Tc.
Results: The mean initial Tc dose was 0.095 $\pm$ 0.002 mg/kg BID. The analysis revealed that recipient's age, BMI, and pretransplant diabetes, but not gender or residual diuresis are explaining the veariability of initial Tc trough level. Recipients >70 years old had 46% greater Tc initial trough levels than those 30 years or less (16.5 $\pm$ 7.1 vs. 11.3 $\pm$ 6.3 ng/ml, p < 0.001). Higher concentrations were also observed in diabetics (16.6 $\pm$ 8.0 ng/ml) than nondiabetics (13.5 $\pm$ 6.7 ng/ml), and in overweight (15.3 $\pm$ 7.0 ng/ml) and obese (16.9 $\pm$ 5.9 ng/ml) than normal weight (13.0 $\pm$ 6.7 ng/ml) and underweight (10.9 $\pm$ 7.2 ng/ml) patients. The association between Tc trough level and BMI was independent from the influence of age. Additionally, there was no influence of early graft function on Tc trough level.
Conclusion: The reduction of recommended fixed Tc initial dose should be considered in the elderly, diabetics, and overweight/obese kidney transplant recipients.

023 KIDNEY

BO191 SHORT-TERM CHANGE IN RENAL FUNCTION BEFORE AND AFTER NEPHRECTOMY OF LIVING KIDNEY DONORS

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Background: Normal renal function has been recognized as an important portion of the living donor's healthy after kidney donation. The purpose of this study was to evaluate the short-term changes in renal function of living donors before and after kidney donation.
Methods: Of 145 living kidney donors from January 2001 to December 2013, we analyzed the data of 58 donors completed the examinations of before nephrectomy and 1, 6 and 12 months follow-up examinations after nephrectomy.
Results: Of 58 donors, female were 53.4%. The mean age was 38.6 ± 12.35 years. In the relationship with recipient, sibling (29.3%) and children (25.9%) were predominant. As the indicators of renal function, BUN, Cr, eGFR, and CCr were analyzed. Before kidney donation, the mean and standard deviation (SD) of BUN, Cr, eGFR, and CCr were 12.85 ± 3.34 mg/dl, 0.85 ± 0.15 mg/dl, 97.76 ± 15.36, and 91.74 ± 15.59 ml/min respectively. At 12 months after nephrectomy, BUN 15.53 ± 3.48 mg/dl, Cr 1.12 ± 0.21 mg/dl, eGFR 71.55 ± 15.8, CCr 68.04 ± 17.15 ml/min. Reviewing the differences in kidney function according to the general nature, Cr in accordance with the gender difference is, but eGFR ratio there was no difference. Group of donation by children and under the age of 30, eGFR ratio results showed significant differences between the highest scores. Analyzing results of an average score 66 points in eGFR ratio after 1 month in donation, there was statistically significant good score a group more than 66 in eGFR ratio such as Cr (before donation, after 6 months), BUN (after 1 month) and eGFR (after 12 months).
Conclusions: In spite of compensation reaction, living kidney donation resulted in reduced renal function after nephrectomy and prolonged renal function recovery till 1 year after nephrectomy. It is required for living kidney donors to be managed continuously and systematically before and after nephrectomy.

BO192 CHANGING FOR IMPROVING THE QUALITY AND SAFETY OF LIVING RELATED KIDNEY TRANSPLANTATION

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Purpose: Using the device of Weck Hem-O-Lok ligating clips (Hem-O-Lok) for ligation of the renal artery during the laparoscopic living-donor nephrectomy (LLDN) has been abandoned since 2011. The purpose of this study is to compare the outcome of using the Weck Hem-O-Lok ligating clips with that of using staplers.
Methods: We changed our policy of ligating the renal artery during LLDN by using Hem-O-Lok to using staplers since 2012 September after listening. Friedman's presentation in ESOT 2012. Previously, we have performed 226 LLDN by using the Weck Hem-O-Lok. After 2012 September, we used one laparoscopic stapler for transecting the renal artery and reloaded the second cartridge for transecting the renal vein. In the sixth case, a mechanical error happened during reloading the second cartridge which caused prolonged warm ischemic time. We then changed to using two laparoscopic staplers without any reloading procedure. The warm ischemic times of the consecutive cases before and after changing the policy were compared and analyzed by the Student *t*-test.
Results: Between 2012 September to 2013 December, 16 LLDN have been done by using laparoscopic staplers. The warm ischemic time (120 ± 65 s) of this group was significantly shorter than that of the group using the Weck Hem-O-Lok (180 ± 65 s, $p = 0.025$).The interviews revealed influencing factors for changing the policy of ligating the renal artery during LLDN included an environment for open discussion, team decision making, donor safety, and the pressure of medical dispute.
Conclusion: In conclusion, creating an environment for open discussion about donor safety and warming from the transplant society were the factors caused change. The warm ischemic time in the stapler group was significantly shorter which may have impact on the graft survival. Adverse events may happened in every surgical device.

BO193 MAXIMISING THE POTENTIAL OF PAIRED KIDNEY DONATION

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Background: Paired living kidney donation (LD) provides an alternative transplant option for incompatible donor-recipient pairs. In the UK the first transplant took place in 2007 within the National Living Donor Kidney Sharing Scheme (NLDKSS). There is variability of transplant rates within these schemes across Europe. We considered outcomes for patients from N.Ireland enrolled in the NLDKSS and options for optimizing transplantation rates.
Methods: Matching run reports for our centre were reviewed and all donor-recipient pairs entered into the NLDKSS from October 2009 to October 2014 recorded. Patient demographics, transplantation rates and clinical outcomes were analysed through review of electronic care records.
Results: 78donor-recipient pairs were entered into NLDKSS with 33patients (42%) transplanted via the scheme. 12matches did not proceed. 36patients (46%) have subsequently been transplanted by other means (16incompatible transplants with same donor, 4incompatible with alternative donor, 4compatible with alternative donor, 1compatible with same poorly matched donor, 1altruistic LD, 10deceased donor). Of the incompatible LD 10were ABOi, 9were HLAi. One was combined HLAi and ABOi and had early graft failure. This patient returned to haemodialysis (HD). In addition 4other patients remain on HD, 3have not yet required dialysis and 2died. To increase opportunities for transplantation in the NLDKSS, 2patients had some unacceptable HLA antigens de-listed (where current antibody levels were low or undetectable), and 2had alternative blood groups listed. This has permitted additional transplants e.g. a very highly sensitized patient successfully received a blood group incompatible, HLA compatible graft.
Conclusion: NLDKSS has contributed to the expansion of the LD programme at our centre with 42% of patients entered being successfully transplanted. We have demonstrated that additional transplants are possible with consideration of higher immunological risk transplants.

BO194 DONOR COMPREHENSION OF PROVIDED INFORMATION DURING INFORMED CONSENT PROCESS IN LIVE DONOR NEPHRECTOMY

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Erasmus MC

Background: Since living kidney donors are a unique group of "patients", undergoing surgery for the benefit of others, safety and informed consent are even more important than in other surgical procedures. Current literature demonstrates great variations in informed consent practices. Donors report varying degrees of satisfaction with the information and preparation for live donor nephrectomy.
Methods/Materials: The preoperative surgical outpatient clinic visits of 46 potential living kidney donors were observed. Provided information was scored using standardized checklists, team members ($N = 9$) received an "informer score" for each consultation. Immediately after giving consent for donor nephrectomy, and again on the day of admission for surgery, donors received a questionnaire testing their knowledge of the upcoming operation. Informers as well as donors could score a maximum of 20 points. Scores were compared between donors and. Outpatient scores were also compared with admission scores. Demographic data and baseline donor characteristics were documented for correlation purposes.
Results: There were marked variations between the information provided by different informers. Median informer score was 12 (range 2–20). Important complications were not always disclosed. Table 1 demonstrates donor scores at the different time intervals (median, range).

	Outpatient Score $N = 46$	Admission Score $N = 27^{\#}$
Overall score	6 (1–10)	6 (2–11)
Surgical technique	1 (0–3)	2 (0–3)
Short term complications	2.5 (0–5)	2 (0–6)
Long term complications	0 (0–2)	0 (0–2)
Duration of admission	1 (0–1)	1 (0–1)
Duration of convalescence	1 (0–1)	1 (0–1)

#19 Donors are still awaiting surgery.

Risk of death was mentioned 42 times (91%) by the surgical team but reproduced by only ten donors (22%). No correlation between any of the donor characteristics and donor comprehension could be demonstrated.
Conclusion: Information provided to potential living kidney donors varies among informers, and relevant details are not always disclosed. Donors never recall all provided information, not even immediately after the surgical consult. A more detailed analysis of the informed consent process is necessary to further improve living kidney donor education and ensure donor satisfaction.

BO195 MORE THAN A DECADE AFTER LIVE DONOR NEPHRECTOMY – A PROSPECTIVE COHORT STUDY

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Background: Previously reported short-term results after live kidney donation, show no negative consequences for the donor. The incidence of new-onset morbidity takes years to emerge, making it highly likely that this will be missed during short-term follow-up. Therefore evidence on long-term outcome is essential.
Methods: A 10-year follow-up on renal function, new onset hypertension, quality of life, fatigue scores, and survival was performed of a prospective cohort of 100 donors.
Results: After a median follow-up time of 10 years, clinical data was available for 97 donors and quality of life data was available for 74 donors. Nine donors died during follow-up of unrelated causes to donation, and one donor was lost to follow-up. There was a significant decrease in kidney function of 12.9 ml/min ($p < 0.001$) after a median follow-up of 10 years. Quality of life showed significant lower baseline scores compared to 10-year follow-up in SF-36 dimensions of physical function domain (−7.0, $p < 0.001$), bodily pain (−7.0, $p = 0.001$), general health (−7.1, $p < 0.001$), and vitality (−4.1, $p = 0.028$), and higher MFI-20 dimensions scores of general fatigue (+2.2, $p < 0.001$), physical fatigue (+2.0, $p < 0.001$), reduced activity (+1.0, $p = 0.019$), and reduced motivation (+0.8, $p = 0.030$) (Table 1). New-onset hypertension was present in 25.6% of the donors (818 person-years). Donor and graft survival, were 91% and 66%, respectively.
Conclusion: Donor outcomes are excellent 10 years post-nephrectomy. Kidney function appears stable and hypertension does not seem to occur more frequently compared to the general population.

Table 1 Quality of life of 74 live kidney donors after 10 years past donation. Raw data at baseline and 10-year follow-up [estimate (SD)]. Estimated adjusted difference between baseline and 10-year follow-up, 95% confidence intervals and p-values for the dimensions of the SF-36 and MFI-20 scales during 10-year follow-up. For the SF-36 dimensions overall scores from the general population with similar age are provided [estimate (SD)].

	Baseline	Ten-year follow-up	General population	Estimated difference	95% Confidence interval	p-value[1]
Dimension						
SF-36						
Physical function	92.5 (13.1)	85.5 (16.0)	84.0 (19.6)	−7.0	−10.9 to −3.2	<0.001
Role physical	91.1 (24.7)	89.0 (30.1)	74.5 (36.8)	−1.4	−9.6 to 6.7	0.728
Bodily pain	95.0 (13.6)	88.0 (16.7)	71.8 (24.1)	−7.0	−11.3 to −2.8	0.001
General health	85.1 (13.7)	78.2 (15.5)	69.7 (20.6)	−7.1	−10.8 to −3.4	<0.001
Vitality	79.9 (15.0)	75.8 (17.0)	68.6 (20.2)	−4.1	−7.8 to −0.5	0.028
Social functioning	90.0 (15.6)	89.2 (17.3)	83.5 (22.1)	−0.8	−4.9 to 3.4	0.716
Role emotional	90.0 (24.1)	91.8 (27.8)	81.6 (33.2)	2.4	−5.2 to 10.0	0.539
Mental health	81.1 (13.2)	82.4 (13.8)	75.6 (18.5)	1.3	−1.5 to 4.1	0.345
MFI-20						
General fatigue	6.0 (3.0)	8.3 (3.9)	8.4 (3.4)	2.2	1.4 to 3.1	<0.001
Physical fatigue	5.5 (2.5)	7.4 (3.4)	7.9 (3.7)	2.0	1.2 to 2.8	<0.001
Reduced activities	6.8 (3.1)	7.8 (3.6)	7.9 (3.5)	1.0	0.2 to 1.8	0.019
Reduced motivation	6.3 (2.5)	7.2 (3.3)	7.8 (3.1)	0.8	0.1 to 1.5	0.030
Mental fatigue	7.4 (4.0)	7.5 (3.9)	7.5 (3.2)	0.1	−0.7 to 0.9	0.807

1Baseline compared with 10-year follow-up.

BO196 DEDICATED GUIDANCE: MULTI-DIMENSIONAL COOPERATION LEADS TO MORE PRE-EMPTIVE KIDNEY TRANSPLANTATION

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Maasstadziekenhuis

Introduction: In time start of the process of education and pre-transplant medical investigations may increase the possibility of pre-emptive (living) renal transplantation. We enrolled a work-up programme by close cooperation between a specialised nurse and the team of social workers in a large non-academic teaching hospital.
Method: The electronic hospital patient form is used to inform all involved disciplines at once. The programme then starts with a home visit by a social worker. At this visit, general information about renal replacement therapy and the possibility of renal transplantation is explained to the patient and accompanying family and friends. The specialised nurse will explain the transplantation options and the medical work-up of the recipient and the potential donor. She further ensures that the required investigations are planned and completed in the shortest possible time frame. Close daily cooperation between the specialised nurse and the team of social workers will optimize the transplantation work-up and can result in a quick change in the process, for instance a change of the potential donor by medical reasons.
Results: In 2013, 79 patients entered the programme. That year, 22 donor-recipient pairs were transferred for transplantation, of which 12 were transplanted by the end of the year. The median work-up time was 169 days (range: 23–639)Several patient and medical factors delayed the programme. They will be discussed at the meeting.

Discussion: By the current transplant work-up programme, patients and family/friends are well informed about renal replacement therapy and the possibility of (living) transplantation. Close cooperation between a specialised nurse and the team of social workers results in a significant improvement of the possibility of pre-emptive renal transplantation or, otherwise, patients are earlier registered on the waiting list.

BO197* THE ADVANTAGES OF UNSPECIFIED LIVING KIDNEY DONATION

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Erasmus MC

Background: In unspecified living kidney donation there is no relationship between donor and recipient and this type of donation is conducted on a strictly anonymous basis. There is not material benefit for the donor.
Methods: From 2000 to 2015, we prospectively collected data of individuals who approached us with the intention to donate a kidney to a patient waiting for a kidney in our centre.
Results: In total 276 potential donors contacted our centre for information about unspecified donation. After a first telephone call, they received a DVD and written information about the consequences of living kidney donation. One hundred eighty-two donors started the screening process, which included a medical and psychological evaluation. For medical and psychological reasons, the procedure was stopped for 26 donors. Twenty-one individuals decided not to donate. Sixteen donors are currently in the screening process. We referred 1 to another centre. One hundred eighteen were put on the waitlist for the donation. After that, 5 decided not to donate, three donors for medical reasons. One hundred six donors enabled 183 kidney transplants. They donated to 77 recipients of incompatible couples in domino paired procedures, and the domino/bridge donors to 64 waitlist recipients. Forty-two unspecified donors donated their kidney anonymously to 42 recipients on the waitlist.

Conclusion: Methods to increase living donation should be encouraged. Unspecified donation makes a significant contribution to the life donation program. Both patients on the deceased donor waiting list and those participating in a kidney exchange program stand to benefit from unspecified donation.

BO198 COMPARISON OF CLINICAL OUTCOMES BETWEEN IN THE SPOUSAL DONOR KIDNEY TRANPLANTS: WIFE TO HUSBAND VERSUS HUSBAND TO WIFE

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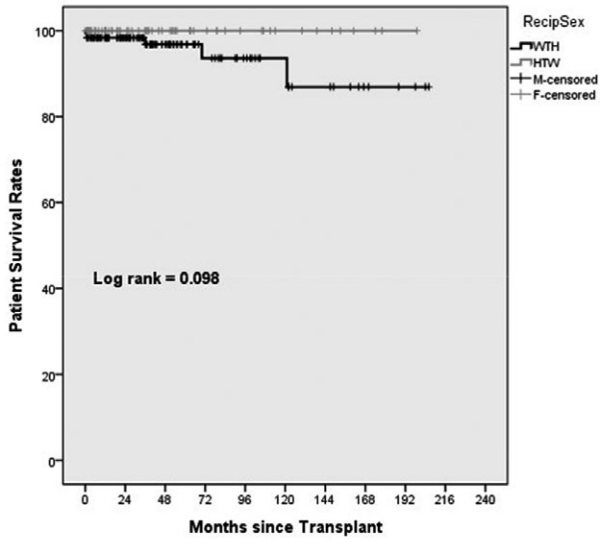
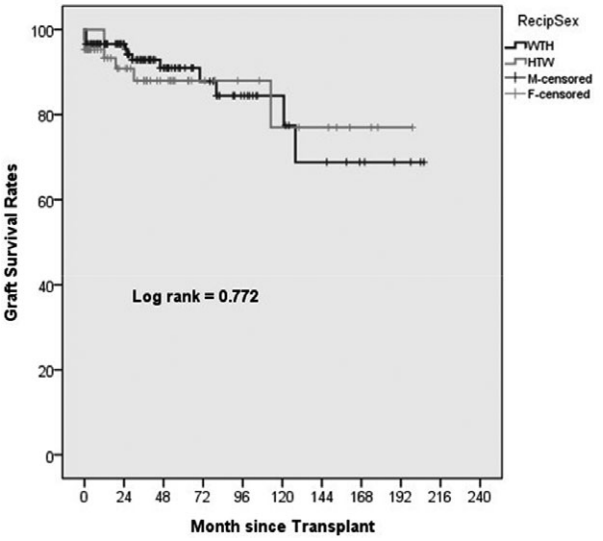
Backgrounds: As the organ shortage is a worldwide problem in kidney transplantaion, use kidneys from living unrelated donor, especially spousal donor is one of the overcomig the organ shortage.However there is few clinical outcome data between the wife-to-husband recipients(WTHr) and husband-to-wife recipients(HTWr).This study was conducted to compare the clinical outcomes between the WTHr and HTWr.
Materials and Methods: This is a retrospective single center study from January 1997 to October 2014. One-hundred eighty three spousal donor kidney transplantations were performed in our institute (119 WTHr vs. 64 HTWr).The clinical characteristic and biopsy-proven acute rejection (BPAR) free survival rates, graft survival rates, and patiens survival rates between spousal transplants were analyzed.
Results: The HTWr demonstrated higher crossmatch positivity (6(5%) vs. 9 (14.1%), $p < 0.01$), and positive panel-ractive antibodies (PRA) (PRA class I 12 (11%) vs. 18 (31%), $p < 0.01$; PRA class II 15 (13.8%) vs. 23 (39.7%), $p < 0.01$) than in WTHr. And nephron mass index(NMI) was higher in HTWr than WTHr, significantly (7.6 vs. 9.3, $p < 0.001$), and mean serum creatinine level was lower in HTWr at all the time points. The 15-years BPAR free survival rates were worse in HTWr (56.6%) than WTHr (72.7%) which was not significant ($p = 0.297$).And 15-years graft survival rates for WTHr and HTWr were not sigificantly different (68.8% vs. 77.0% repectively, $p = 0.772$), and patient survivial were similar in both group (93.6% vs. 100% repectively, $p = 0.098$).
Conclusion: In our study the BPAR free survival rates showed worse outcome in HTWr ($p = 0.297$), and immunogic factors (crossmatch-positive nad PRA-positive) were hostile in HTWr. However graft survivcal rates and the patient survival rates were similiar in both groups. One possible explanation for these results, is the positive effect of NMI on graft survial, that NMI checked higher in HTWr significantly. The NMI may offset the negative effect of immunologic factor in HTWr.





BO199 RENAL FUNCTION AND MORBIDITY IN ELDERLY DONORS AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: The risk of end-stage kidney disease in carefully screened living kidney donors (LKD) is similar to the general population. We aimed to evaluate the outcomes and 1-year kidney function of elderly LKD.
Method: A retrospective study was performed based on a prospective database of all consecutive LKD who underwent laparoscopic nephrectomy for living donor kidney transplantation (LDKT) at a single tertiary center (September 1998–December 2013). The cohort was divided into donors' ≥60 years old (Elderly) and <60 years old (Young). Renal function was assessed by creatinine levels and respective estimated glomerular filtration rates (eGFR). Complications were classified according to the Dindo-Clavien classification.
Results: In a total of 213 LKD, 49 were Elderly and 164 Young. Median age was 66 (range: 60–79) and 46 years (range: 25–59), respectively. Female to male ratio was 67% in both groups. Mean operative time (149 vs. 152 min, $p = 0.69$), conversion rate to laparotomy (2 vs. 1.8%, $p = 0.92$), grade III-IV complications (4.1 vs. 1.8%, $p = 0.36$) were similar. However, Elderly had more grade I-II complications (18 vs. 4%, $p < 0.0001$). Despite similar pre-donation eGFR values (80 vs. 84 ml/min/1.73 m^2), elderly presented significantly lower eGFR during the inpatient period (45.8 vs. 51.5 ml/min/1.73 m^2, $p = 0.0003$),

at 1 month (51 vs. 58 ml/min/1.73 m^2, p = 0.002) and at 1 year (54 vs. 62 mL/min/1.73 m^2, p = 0.001).
Conclusion: The surgical outcomes of LKD ≥60 years are acceptable and similar to the young, except for minor complications. Despite renal function improvement over the first year, elderly donors tend to present a lower eGFR at 1 year after donation. This study will pave the way to further prospective studies assessing the long-term renal function of elderly LKD.

BO200* EVALUATION OF LIVING KIDNEY DONORS, IS THE SPLIT FUNCTION ISOTOPE TEST USEFUL?

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Introduction: Live Donor Kidney Transplantation (LDKT) remains the gold standard treatment for end stage renal failure (ESRF) due to excellent graft and patient survival. BTS guidelines stipulate that measurement of estimated glomerular filtration rate (eGFR) must be assessed prior to donation. In addition CT angiography, followed by isotope scanning are performed if there is a >2 cm size difference between the kidneys to assess anatomy and differential function.
Aims: To investigate the role of isotope scanning in the decision making process in LDKT.
Methods: Retrospective analysis of live kidney donors (Jan 2012–Dec 2013) at a single centre was performed. All donors underwent medical assessment and CT angiogram and isotopic GFR split function test.
Results: The investigations for 119 patients (mean age 49 SD12 years; 54.6% female and the median isotope GFR 90 mls/min/1.73 m^2 (range 64 – 116) were reviewed. CT angiography showed the median size of left and right kidneys were 10.8 cm (range 8.4–13.5 cm) and 10.7 cm (range 8.4–13.4 cm) respectively. The median split function was 50% bilaterally (range 41–59%). There was a significant correlation of kidney size with split function $r = 0.3$ (p = 10% difference in split function, none of these cases had a size discrepancy >2 cm. Of 119 donors, only one had >2 cm size difference on CT angiogram (L9 cm, R11 cm), but the split function was 10% indicating that few donors fall into this category.
Discussion: The results of this study confirm reports that a CT angiogram, which provides anatomical information as well as size, can be used to evaluate and predict the function in the majority of living donors without the isotope GFR split function test potentially generating both temporal and financial savings.

025 LIVER

BO201* ACUTE KIDNEY INJURY IN THE MELD ERA OF LIVER TRANSPLANTATION. ARE CALCINEURIN INHIBITORS SO PROBLEMATIC FOR RENAL FUNCTION?

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Background: Acute kidney injury (AKI) after liver transplantation(LT)is a common problem. Calcineurin inhibitors(CNI) have to be well-balanced. The aims were analyze the specific effect of CNI on AKI in a large cohort of patients and analyze the profile of AKI-RIFLE categories in the post-transplant setting and its impact on post-transplant-survival.
Methods: A retrospective analysis of 400 patients transplanted at Reina Sofia-Cordoba and King's College Hospital-London was performed. Exclusion criteria were paediatric transplants, death<14 days and CNI-free regimes.Endpoints were: Development of AKI and 1-year survival.
Results: A total of 330 patients were included. Incidence of AKI-Risk-Injury-Failure in the first 2 weeks after LT was 59.8%, 34.3% and 8.4%, respectively. The development of any AKI had no impact on overall 1-year survival. In the multivariate analysis, intraoperative transfusions (OR = 1.15[1.04–1.3]), peak-post-transplant-transaminases (OR = 2.9[1.01–8.77], pretransplant eGFR (OR = 10.54 [1.88–59.1]) and normal-CNI-dose strategies OR = 0.29 [0.14–0.61]) were independent predictors of AKI_Risk. Similarly, peak post-transplant-transaminases (OR = 3.3 [1.39–7.8]) and normal-CNI-dose strategies (OR = 0.31 [0.15–0.62]) were predictors of AKI_Injury. Only peak post-transplant-transaminases (OR = 6.8 [2.6–16.8]) was a predictor of AKI_Failure. In the general linear models, renal-protective strategies with low-CNI doses were only useful to prevent severe impairment in patients with extremely-low pre-transplant eGFR, being useless in the rest.
Conclusions: AKI is frequent after LT. Transfusion, immediate liver function, pretx status and IS are factors that predict mild AKI. However, only immediate liver function predicts severe AKI. AKI happens similarly in all pre-tx eGFR status groups. Low CNI regimes are mildly useful in severely impaired eGFR pretx ststatus patients being useless when pretransplant normal kidney function is preserved.

BO202 DE NOVO ONCE-DAILY TACROLIMUS IN LIVER TRANSPLANTATION: LONG-TERM OUTCOMES OF A SINGLE CENTER COHORT OF 150 PATIENTS

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Purpose: To describe for the first time the long-term safety and efficacy profile of de novo once-daily tacrolimus (Tac QD) in orthotopic liver transplantation (OLT)
Patients and Methods: A retrospective study was conducted including 150 consecutive adult OLTs treated with de novo Tac QD at our institution between April 2008 and March 2011. Recipients were followed-up until December 2014. Initial dose of Tac QD was 0.15 mg/kg/day or 0.1 mg/kg/day when Tac QD was combined with MMF. Renal function was evaluated using estimated glomerular filtration rate based on MDRD-4 formula.
Results: Median age of recipients was 55.5 years (range 20–67). Primary disease leading to OLT was alcoholic cirrhosis in 47.3% of the patients, hepatitis C in 30.6%, hepatitis B in 5%, cholestatic disease in Median MELD score was 15 (r 8–40). Fifty-nine patients had hepatocellular carcinoma (HCC). Antibody induction was used in 17.3% of the patients, steroids in 81.3% and MMF in 36%. Median follow-up was 45.6 months (r 1–76). Median tacrolimus trough levels during the first week and at 1, 3 and 5 years after OLT were 7.85 (*r* 1.9–32.5), 6.5, 4.8 and 4.5 ng/ml, respectively. Acute cellular rejection ocurred in 17 patients (11.3%). During follow-up, chronic renal dysfunction was observed in 23 patients (15%) arterial hypertension in 29 (19.3%) and diabetes mellitus in 21 (14%). Infection rates during hospitalization and after discharge was 17.3% and 22.2%, respectively. Cytomegalovirus infection accounted for 44.8% of all infections. Seven patients developed de novo tumors (4.7%). Retransplantation rate was 5.3%. Pretransplant, 1-, 3- and 5-years posttransplant mean creatinine clearance was 98.7, 77.7, 79.3 and 74.8 ml/min/1.73 m^2, respectively. Patient survival at 1, 3 and 5 years was 96.6%, 92.5% and 87.8%, respectively.
Conclusion: Immunosuppression based on de novo once-daily tacrolimus in adult OLT is effective and safe at the long-term with outstanding patient survival.

BO203 ADOPTIVE IMMUNOTHERAPY WITH ACTIVATED NK CELLS EXTRACTED FROM A LIVER ALLOGRAFT PERFUSATE COMPENSATES FOR THE GENETIC SUSCEPTIBILITY TO BLOODSTREAM INFECTION AFTER LIVER TRANSPLANTATION

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Background: In liver transplantation (LT) recipients with an immunosuppressive condition, the innate components of cellular immunity such as natural killer (NK) cells, macrophages and neutrophils play an important role in protecting against infections. Hence, genetic polymorphisms of the immunoregulatory molecules expressed on those cells may lead to the development of severe infectious complications after LT.
Methods: The single nucleotide polymorphisms (SNPs) of FcγRIIa [131H/R] and FcγRIIIa [158F/V] genes were determined in 89 LDLT recipients. We analyzed the relationship between those SNPs and postoperative infectious complications within 30 days after LT.
Results: Consistent with a lower affinity isoform encoded by FCGR3A [158F] to both IgG1 and IgG3, the higher incidence of bloodstream infections (BSI) was observed in the FCGR3A [158F/V or F/F] than the FCGR3A [158V/V] patients (28.9% vs. 9.1%, p = 0.029). In addition, the incidence of BSI tended to be higher in the patients with the FCGR2A [131H/H] (distinguished by its low affinity for CRP) than those with FCGR2A [131H/R or R/R]. In a separate phase I trial on 31 patients with HCC, we successfully performed adoptive immunotherapy by using IL-2-activated NK cells extracted from a liver allograft perfusate 3 days following the LT. In the cohort of FCGR3A [158F/V or F/F] patients, the incidence of BSI was lower in the patients with immunotherapy than those without immunotherapy, and the survival rate was improved in the patients compared to controls (BSI ratio: 6.3% vs. 15.8%; survival: p = 0.031). Such a potentiating effect of the immunotherapy was not observed in the FCGR3A [158V/V] patients, who were genetically resistant to infectious complications.
Conclusions: FcγR SNPs help in predicting the susceptibility of LT recipients to BSI. In addition, adoptive immunotherapy with activated NK cells can compensate for the genetic susceptibility to BSI and improve the survival rate of patients after LT.

BO204 EVEROLIMUS WITH REDUCED TACROLIMUS PROVIDES IMPROVED RENAL FUNCTION IN LIVER TRANSPLANT RECIPIENTS: A MELD SCORE SUBGROUP ANALYSES FROM THE RANDOMISED-CONTROLLED H2304 STUDY AT MONTH 12 AND 24

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Purpose: The H2304 study showed that everolimus (EVR) provides similar efficacy and superior renal function compared with standard tacrolimus (TAC-C) in *de novo* liver transplant recipients (LTxR). Here, we present the efficacy and safety outcomes at month (M) 12 post-LTx from the pre-planned subpopulation analyses based on the model for end-stage liver disease (MELD) scores.
Methods: H2304 is a 24-M, multicentre, open-label, randomised study that compared the efficacy and safety of EVR (C0 3–8 ng/ml) + reduced-exposure tacrolimus (C0 3–5 ng/ml; EVR+rTAC) or EVR (C0 6–10 ng/ml) with TAC withdrawal (TAC-WD) at M4 to TAC-C (C0: 6–10 ng/ml); all arms include corticosteroids. Following 30 ± 5 day run-in period with TAC-based immunosuppression (± mycophenolate), LTxR were randomised 1:1:1 to the 3 arms. Primary endpoint at M12 was the composite efficacy failure rate of treated biopsy-proven acute rejection (tBPAR), graft loss or death. Secondary endpoint was evolution of renal function using estimated glomerular filtration rate (eGFR; measured by Modification of Diet in Renal Disease 4 [MDRD4]).
Results: At M12 and M24, the composite efficacy failure rates across MELD scores were similar in both the arms. Lower incidence of tBPAR was observed in the EVR+rTAC arm versus TAC-C arm. The eGFR at M12 and M24 was better with EVR+rTAC even in the highest MELD score category. The overall safety profile of both the arms was similar across MELD scores.
Conclusions: Across MELD categories including MELD ≥30, M12 and M24 data from the H2304 study showed that both treatments were equally effective in terms of rejection with EVR showing a benefit of better renal function. The overall safety profile was comparable between treatment arms. The results were similar to the overall population. Since patient numbers are small in the highest MELD categories, results should be interpreted with caution; warranting further research.

Table: Efficacy and safety parameters at Month 12 and 24; overall population and by MELD score subgroups

Parameters*	Treatment	MELD score					
		≤19	20–24	25–29	≥25	≥30	Overall population
Patients (ITT population), n (%)	EVR+rTAC	130 (53.1)	55 (22.5)	31 (12.7)	55 (22.5)	24 (9.8)	245
	TAC-C	128 (52.7)	55 (22.6)	41 (16.9)	58 (23.9)	17 (7.0)	243
Month 12							
Incidence of composite efficacy failure (ITT), n (%)	EVR+rTAC	7 (5.5)	5 (9.5)	4 (12.9)	5 (9.2)	1 (4.3)	16 (6.7)
	TAC-C	13 (10.5)	4 (7.3)	4 (10.1)	6 (10.8)	2 (12.5)	23 (9.7)
Incidence of tBPAR (ITT), n (%)	EVR+rTAC	4 (3.2)	1 (2.1)	3 (9.9)	3 (5.6)	0 (0.0)	7 (2.9)
	TAC-C	9 (7.3)	3 (5.5)	4 (10.1)	5 (9.0)	1 (6.7)	17 (7.0)
Incidence of graft loss or death (ITT), n (%)	EVR+rTAC	4 (3.2)	4 (7.6)	3 (9.7)	4 (7.4)	1 (4.3)	12 (4.9)
	TAC-C	4 (3.3)	1 (1.9)	1 (2.6)	2 (3.6)	1 (6.3)	7 (2.9)
eGFR at M12 (mL/min/1.73m^2, MDRD4; ITT), mean (SD)	EVR+rTAC	85.48 (26.20)	74.72 (26.32)	67.63 (23.42)	72.01 (27.66)	77.20 (31.73)	80.9 (27.31)
	TAC-C	71.11 (22.15)	69.86 (23.72)	69.36 (27.96)	69.52 (25.34)	69.87 (18.91)	70.3 (23.12)
Month 24							
Incidence of composite efficacy failure (ITT), n (%)	EVR+rTAC	13 (10.6)	6 (11.6)	4 (12.9)	5 (9.2)	1 (4.3)	24 (10.3)
	TAC-C	17 (14.0)	5 (9.2)	5 (12.8)	7 (12.7)	2 (12.5)	29 (12.5)
Incidence of tBPAR (ITT), n (%)	EVR+rTAC	6 (5.0)	2 (4.4)	3 (9.9)	3 (5.6)	0 (0.0)	11 (4.8)
	TAC-C	10 (8.2)	3 (5.5)	4 (10.1)	5 (9.0)	1 (6.7)	18 (7.7)
Incidence of graft loss or death (ITT), n (%)	EVR+rTAC	8 (6.6)	5 (9.7)	3 (9.7)	4 (7.4)	1 (4.3)	17 (7.3)
	TAC-C	9 (7.7)	2 (3.8)	2 (5.3)	3 (5.5)	1 (6.3)	14 (6.2)
eGFR at M24 (mL/min/1.73m^2, MDRD4; ITT), mean (SD)	EVR+rTAC	78.52 (24.74)	70.05 (24.90)	62.75 (24.52)	67.84 (27.89)	73.43 (30.85)	74.7 (26.13)
	TAC-C	69.33 (21.05)	64.57 (17.19)	68.43 (27.04)	68.21 (24.84)	67.60 (18.74)	67.8 (21.02)

*All the efficacy parameters are reported as Kaplan-Meier estimates; estimated glomerular filtration rate; EVR, everolimus; ITT, intent-to-treat; M, month; MDRD4; modification of diet in renal disease; MELD, model for end-stage liver disease; rTAC, reduced-dose tacrolimus; SD, standard deviation; TAC-C, tacrolimus control.

BO205 COST SAVING OF IMMUNOSUPPRESSION WITHDRAWAL AFTER LIVER TRANSPLANTATION IN A SPENDING REVIEW ERA

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Background: Clinical tolerance is defined as stable normal graft function in the total absence of a requirement for maintenance immunosuppressive drugs, and may be achieved in up to 20% of very well selected liver transplant recipients. In this observational prospective bi-centric study we evaluated the safety of long-term immunosuppression (IS) off and the cost effectiveness of sustained IS withdrawal after LT.
Methods: Thirty-five LT recipients (mean age: 51 ± 11.9 years, M/F:30/5) transplanted at Tor Vergata University in Rome and Hospital Saint Luc in Brussels completed withdrawal of IS after a mean follow-up from LT of 89.8 ± 63.8 months. The cirrhosis HCV related was the indication in 12 (34%) patients. The safety of IS withdrawal was evaluated according to: a) patients and graft survival; b) liver function tests, obtained at baseline and the last clinical follow-up; c) acute or chronic rejection at the last biopsy. The cost effectiveness of immunosuppression withdrawal was calculated on the basis of the time elapse without therapy according to the actual National Health Service drugs costs.
Results: The mean follow-up of sustained weaning off was 100.3 ± 63.1 months. No difference was observed in relation to transaminase and bilirubin levels. Increase of GGT was noted between baseline and last follow up values [52.8 ± 53 vs. 108.4 ± 114.1 UI/l (p = 0.006)]. At the last available biopsies no patient showed signs of acute or chronic rejection. The 10 years patients and graft survival were 91.4%. Three patients died due to LT unrelated causes. The withdrawal of IS drugs in this small tolerant patient cohort represents 674.239 € (81.925 €/yearly) of saving.
Conclusion: Complete and permanent IS withdrawal could be achieved after LT without compromising outcome in terms of survival and liver function. This strategy represents a great saving on the public health economy.

BO206* CONVERSION TO EVEROLIMUS (EVL) AFTER LIVER TRANSPLANTATION (LT) IN THE REAL LIFE: DATA FROM THE EVEROLIVER MULTICENTER REGISTRY

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Everolimus (EVL) has been approved for use in de novo LTx recipients. The aim of this multicenter study is to analyze the current reasons for conversion, modalities of use, efficacy and safety in the real life practice.
Methods: From 2006 till 2012, 557 LTx patients from 10 centers were switched to EVL. Data were collected every 3 months the 1st year then every 6 months.
Results: Adult recipients (74.2% male) had a mean age of 53 ± 10 years. Mean delay between LTx and introduction of EVL was 4.5 ± 5.4 years {median: 2.2(0–26 years)}. Immunosuppressive regimen at time of introduction of EVL was steroids (39%) in combination to tacrolimus (79%) or cyclosporine (18%), MMF (51%) and MPA (14%). The reasons of introduction of EVL were chronic renal failure (34.9%), treatment of recurrent HCC (7.1%) or de novo cancer (19.7%), prevention of HCC recurrence (14.9%) and various other reasons related to CNI side effects. EVL was introduced with a median dose of 2 mg/day. CNI were withdrawn in 39.6% and 62.9% of the patients respectively at M3 and M12. In the group of patients with an eGFR at baseline 60 ml/mn/1.73 m^2 (n = 260) median time from transplant to conversion was 15.8 months, mean eGFR at M24 and M36 did not differ statistically from baseline. In the group of patients with a chronic renal failure stage 3 at baseline (eGFR <60 ml/mn/1.73 m^2; n = 245) median time from transplant to conversion was 34.9 months, mean eGFR improved statistically from 43.3 ± 9.8 at baseline to 48.2 ± 16.8 ml/mn/1.73 m^2 at M24; p = 0.006). Nine patients (1.6%) developed a histologically proven acute rejection with a median delay of 3.8 months (1.3–30.8). Patient survival rates of the global population at 1 and 2 years were respectively 91% and 83%.
Conclusion: This real life registry showed that late conversion from CNI to EVL allowed a significant weaning of CNI and a significant improvement of GFR in patients with chronic renal failure with a very low risk of rejection.

BO207 CONVERSION FROM A TWICE-DAILY TACROLIMUS-BASED REGIMEN TO ONCE-DAILY TACROLIMUS EXTENDED-RELEASE FORMULATION IN STABLE PEDIATRIC LIVER TRANSPLANT RECIPIENTS: EFFICACY, SAFETY, AND IMMUNOSUPPRESSANT ADHERENCE

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Background: Recently, an extended-release tacrolimus (TAC-OD) formulation allows once-daily administration that may improve adherence. The aim of the study was to assess the safety and efficacy of conversion (CON) from twice daily TAC (TAC-BID) to TAC-OD in stable recipients of Pediatric Liver Transplant (PLT). METOTHS/MATERIALS: Retrospective review of data of PLT recipients who were converted from TAC-BID to TAC-OD between 2008 and 2015. TAC-OD was started in stable PLT recipients with >1 year of follow-up and a calculated glomerular filtration rate (cGFR) >60 ml/min/m^2 at least 6 months pre-CON. TAC levels, liver and kidney function and blood count were assessed pre-CON, at 7 days and 1-6-12 and 36 months post-CON. Patients were converted to TAC-OD on a 1:1 basis for their daily dose. Adherence was assessed with a visual analog scale (VAS) pretreatment and 1 year after CON.
Results: 43 patients were included (60.9% male) with mean age of 9.6 ± 3.0 years. CON was performed 5.9 ± 3.1 years after LT with a mean follow-up of 4.1 ± 2.4 years. The mean TAC dose was 0.12 ± 0.09 mg/kg before CON and 0.12 ± 0.09, 0.16 ± 0.01 and 0.13 ± 0.08 mg/kg at 6-12-36 months respectively. Mean TAC levels were 4.9 ± 2.0 pre-CON and 4.2 ± 1.7, 4.3 ± 1.8 and 4.1 ± 1.4 ng/ml at 6-12-36 months respectively. TAC dose was increased to maintain therapeutic levels in 46.5%. The increase was higher in patients who performed the CON from TAC suspension than from tablets (40.5% vs. 5.6%; p < 0.0065). Eleven patients had a cGFR between 60–80 ml/min/m^2 pre-CON. All of them improved their cGFR compared to baseline at 1 and 3 years respectively (73.8 ± 4.2 vs. 82.3 ± 7.0 and 117 ± 7.0 ml/min/m^2; p < 0.05). A no-significant improvement was observed in patient adherence (VAS from 82 ± 12.1 to 92.6 ± 7.5; p < 0.07). No patient presented acute rejection or serious adverse effects that lead to TAC-OD discontinuation.
Conclusion: Conversion to TAC-OD appears to be safe and effective in stable PLT recipients.

BO208 EARLY TREATMENT WITH CMV-HYPERIMMUNOGLOBULIN IMPROVES OUTCOME IN HIGH-MELD (≥30) LIVER TRANSPLANT PATIENTS

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Background: Liver transplantation (LT) in patients with high model of end-stage liver disease (MELD) scores is associated with increased risk of infectious and immunologic complications. Unspecific / specific immunoglob-

ulines (Ig) were in the past shown to provide beneficial immuno-modulatory capabilities. The aim of this pilot trial was to assess the impact of early post-LT treatment with CMV hyperimmunoglobulin (CMVIg) on early post-LT outcome in high-risk (MELD ≥30) patients.
Material/Methods: A total of 32 liver transplant patients with a median MELD score of 38 (range: 30–40) were included. Based on CMV risk constellation (recipient + or donor +), CMVIg (Cytotect, Biotest, Germany) was administered at a dose of 3 × 5000 IE during 1 week post-LT. The impact of CMVIg treatment along with other paramters on outcome was analyzed by uni- and multivariate analysis.
Results: Nineteen patients were ICU-bound (59.4%), 15 patients required ventilation (46.9%), 11 patients were on dialysis (34.4%), and 16 patients needed catecholamines (50%) at LT, respectively. Risk triad (ventilation + dialysis + catecholamines) was documented in 11 patients (34.4%). Twenty-one patients have received CMVIg (65.6%), while 11 liver recipients did not. In univariate analysis, patients' age ($p = 0.005$), ΔMELD ($p = 0.024$), lactate-level at LT ($p = 0.001$), ventilation at LT ($p = 0.009$), catecholamines at LT ($p = 0.023$), risk triad at LT ($p = 0.03$), CRP-level at LT and CMVIg treatment post-LT ($p < 0.001$) were correlated with poor outcome. Donor characteristics did not affect outcome. In multivariate analysis, only pretransplant CRP-level ≤4 mg/dl and post-LT treatment with CMVIg were independent predictors of beneficial outcome. Survival rates at 3- and 6-months were 95.2% and 85.7% in patients receiving CMVIg, but 54.5% and 36.4% in those without CMVIg therapy ($p < 0.001$).
Conclusion: Treatment with CMVIg might provide beneficial immuno-supporting properties in high-MELD liver recipients.

BO209 OUTCOMES OF LIVING DONOR LIVER TRANSPLANTATION ALONE WITH MAINTENANCE RENAL REPLACEMENT THERAPTY IN JAPAN: A MULTI-INSTITUTIONAL STUDY OF THE JAPANESE LIVER TRANSPLANTATION SOCIETY

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Background: Since simultaneous live and kidney transplantation has been limited as a standard practice because of a severe shortage of deceased donors in Japan, living donor (LD) liver transplantation alone (LTA) is indicated in most recipients with maintenance renal replacement therapy (MRRT). The aim of this study was to clarify the result of LTA in patients with MRRT.
Materials/Methods: All data were collected retrospectively from thirteen Japanese institutes which experienced LD LTA for MRRT patients. All recipients were on MRRT before LTA. Characteristics of donors and recipients, postoperative complications, survival rate, and causes of death were analyzed. Data for thirty-five patients including seven pediatric patients were collected.
Results: In adult cases ($n = 28$), overall survival rate at 1 and 5 year was 66.1% and 57.3%, respectively. In the seven pediatric cases, overall survival rate at 1 and 5 years was both 83.3%. Six recipients died of sepsis within 6 months after LD LTA. Three adult recipients died of non-aneurysm cerebral hemorrhage after 1 year and one recipient died of acute heart failure after 7 months. As to postoperative complications, infection (bacterial, viral, and fungal) was detected in fifteen recipients (50%). Secondary kidney transplantation from LD was performed in five adults and four pediatric recipients after primary LTA. In adult recipients, graft weight versus standard liver volume, duration and blood loss in LTA surgery were associated poor outcomes after LD LTA. Postoperative spontaneous withdrawal of MRRT was detected in only one adult case.
Conclusion: Early post-LD LTA mortality seemed higher in patients with MRRT as compared to those without MRRT with characteristic causes. For pediatric MRRT patients, LTA prior to kidney transplantation could be considered acceptable treatment. Smaller graft for size and complicated surgery were associated with poor outcome after LD LTA.

BO210 SUCCESSFUL PROTOCOL WITH RITUXIMAB IN ADULT LIVING DONOR LIVER TRANSPLANTATION ACROSS ABO BARRIER

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Background: Survival in adult ABO-incompatible living donor liver transplantation has been improved by portal or arterial infusion therapy, and anti-CD20 agent (Rituximab). However, catheter related complication or infection due to overimmunosuppression is always at risk.
Methods: We performed eight cases of ABO-incompatible living donor liver transplant. We administered Rituximab in all cases 2–3 weeks before transplantation, and plasma exchange was indicated before operation in case of antibody titer x16≤. Splenectomy was indicated on a case-by-case basis. We started methylprednisolone (mPSL) and prostaglandin E1 (PGE1) infusion via hepatic arterial catheter, or systemic administration of mPSL. Mycophenolate mofetile (MMF) was added to the immunosuppressants in all cases.
Results: B lymphocytes (CD19+cells) had been suppressed to almost 0% during perioperative period by the single administration of Rituximab. Antibody titer recovered in 1–2 weeks after operation, though it is unclear whether or not it is related to humoral rejection. Although arterial infusion therapy was not adopted in the latter five cases or PGE1 was not given in two cases, no one experienced humoral rejection and all patients survived the ABO-incompatible liver transplant. Symptomatic cytomegalovirus infection occurred in one case. However, serious opportunistic infection was not found in any case.
Conclusion: Arterial infusion therapy can be omitted by Rituximab use. And, PGE1 also can be excluded from the immunosuppressive treatment for ABO-incompatible transplant. It seemed that simple systemic adminstration of steroid and PGE1 is not inferior to arterial infusion therapy in the era of Rituximab. Immunosuppressive regimen with Rituximab is promising for ABO-incompatible living donor liver transplant.

Case	Age, Gender	Original Disease	Donor, ABO	Titer, IgM/IgG	Pre-LTx @CD20	Pre-LTx apheresis	mPSL, PGE1	Arterial infusion	Splenectomy
1	35, F	Wilson	Husband, A to B	x128/x64	Yes	Yes	mPSL, PGE1	Yes	Yes
2	64, F	HCV-LC	Son, A to O	x32/x128	Yes	Yes	mPSL, PGE1	Yes	Yes
3	55, M	HCV-LC	Wife, A to O	x64/x128	Yes	Yes	mPSL, PGE1	Yes	Post-splenectomy
4	58, M	HBV-LC	Son, A to O	x64/x128	Yes	Yes	mPSL	No	No
5	32, M	Biliary atresia	Mother, A to O	x64/x64	Yes	Yes	mPSL	No	Yes
6	58, F	PBC	Son, AB to B	X16/x2>	Yes	No	mPSL, PGE1	No	Yes
7	53, F	PBC	Son, B to O	x256/x256	Yes	Yes	mPSL, PGE1	No	Yes
8	39, M	HCV-LC	Sister, A to B	x32/x4	Yes	Yes	mPSL, PGE1	No	Yes

003 CLINICAL IMMUNOSUPPRESSION & BIOLOGICALS

BO211 PK AND PHARMACOGENOMICS OF ONCE-DAILY MELTDOSE® TACROLIMUS (ENVARSUS® XR) VERSUS TWICE-DAILY TACROLIMUS: A RANDOMIZED CROSS-OVER STUDY IN STABLE AFRICAN AMERICAN KIDNEY TRANSPLANT PATIENTS (ASERTAA)

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Envarsus® XR is a once-daily tacrolimus (tac) that has shown increased bioavailability, lower peak and less peak-to-trough fluctuation at a lower daily dose vs. twice-daily tac (Prograf®), with noninferior efficacy and similar safety. The CYP3A5*1 genotype, highly prevalent in African Americans (AA), commonly necessitates higher tac dose requirements and may hinder efforts to obtain therapeutic drug levels. This may be one reason for the consistently inferior outcomes observed in AA kidney transplant recipients versus other subpopulations, most of whom do not express CYP3A5*1 genotypes. A pooled analysis of phase 3 trial data in de novo and stable black kidney transplant recipients showed a significantly decreased treatment failure risk for Envarsus XR versus Prograf. In this randomized, open-label, two-sequence, three-period crossover study, the steady state PK of once-daily Envarsus XR to twice-daily tac in 50 stable AA kidney recipients will be compared. Secondary objectives include analyzing the PK impact of polymorphic genotype expression, and comparing safety and efficacy. Fifty stable AA kidney transplant recipients will be randomly assigned to continue on twice-daily tac on days 1–7 then switch to Envarsus® XR (at 15% lower dose); or to receive Envarsus® XR on days 1–7 then switch back to twice-daily tac; half each of the patients in each group will comprise those requiring <0.15 mg/kg/day and those requiring ≥0.15 mg/kg/day. Patients completing the PK treatment period may participate in an extension study, continuing on the assigned treatment for up to 6 months. Data on the first 15 patients show that Envarsus XR is significantly associated with lower Cmax (16.2 vs. 26.3 ng/ml, $p < 0.0001$), and similar Cmin (5.9 vs. 5.6 ng/ml, $p = 0.440$) and AUC (242.4 vs. 230.8 h*ng/m, $p = 0.416$). The improved PK and lower total daily dose requirements associated with Envarsus® XR vs. twice-daily tac may also be applicable in AA. Full cohort of PK/PG results will be available mid-2015.

BO212 POOLED ANALYSIS TO EXAMINE THE PK AND SAFETY OF ONCE-DAILY EXTENDED-RELEASE MELTDOSE® TACROLIMUS TABLETS (ENVARSUS®) VS. TWICE–DAILY TACROLIMUS (PROGRAF®) IN DE NOVO KIDNEY AND LIVER TRANSPLANTATION

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Envarsus is a prolonged-release, once-daily, MeltDose tacrolimus formulation that has shown improved PK and similar efficacy and safety as twice-daily Prograf. This pooled analysis of data from 2 Phase II, open-label, parallel-group, multicenter, randomized 12 month trials compared drug dosing, dose adjustments, efficacy and safety between Envarsus and Prograf across de novo kidney and liver transplantation. Patients in both studies were randomized to Envarsus once-daily (kidney, 0.14 mg/kg/day [0.17 for African Americans (AA)]; liver, 0.07–0.11 mg/kg [0.09–0.13 mg/kg for AA]) or Prograf twice-daily (kidney, 0.2 mg/kg; liver, 0.10–0.15 mg/kg). Included were 121 ($n = 63$ kidney; $n = 58$ liver) randomized patients (Envarsus, $n = 61$; Prograf, $n = 60$). The correlation between AUC and Cmin was statistically significant ($p < 0.0001$) at each time point (Table). Across organs the mean total daily dose of both drugs decreased progressively after the first 2 weeks. Dose adjustments were frequent for both drug groups during the first 14 days and were significantly ($p = 0.0015$) less frequent for Envarsus (mean: 3.3/patient) vs. Prograf (4.6/patient). In the first 6 months, mean dose adjustments per patient were Envarsus: 9.4 and Prograf: 11.5. Over the 12 month study, dose adjustments remained fewer for Envarsus. In both groups 63% of adjustments were due to out-of-range trough levels, and 4% due to adverse events (AE). The proportion of pooled patients with treatment failure was similar (3.3% both groups). Except for 1 kidney recipient in the Prograf group, all patients experienced ≥1 AE; 53% of pooled patients in both drug groups experienced serious AEs. Most AEs were mild or moderate and did not lead to study discontinuation. Envarsus showed a comparable efficacy and safety in both de novo liver and kidney transplantation with the potential for fewer dose adjustments vs. Prograf. Pooled analysis further confirms the similarities across both de novo kidney and liver transplants.

Table 1 Dose Normalized Linear Correlation between AUC and C_{min}

	Envarsus	Envarsus	Prograf	Prograf
	Kidney	Liver	Kidney	Liver
Day 1	0.71	0.73	0.76	0.86
Day 7	0.96	0.93	0.87	0.89
Day 14	0.99	0.96	0.98	0.93

BO214 POPULATION PHARMACOKINETICS OF TACROLIMUS IN STABLE PAEDIATRIC RENAL TRANSPLANT RECIPIENTS TRANSLATED INTO CLINICAL PRACTICE

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Background: The aim of this study was to develop a population pharmacokinetic model of tacrolimus in paediatric patients at least 1 year after renal transplantation. We aimed to identify factors contributing to the variability of tacrolimus pharmacokinetics and determine individualised dosage regimens.
Patients and Methods: We included 45 children with 120 2- or 4-h profiles. The median age at baseline was 11.1 years (range: 3.8–18.4) and the median time since transplantation 16.2 months (range: 11.4 – 124). The pharmacokinetic analysis was performed using the non-linear mixed-effects modelling software (NONMEM). The impact of covariates including concomitant medications, age, CYP3A5 and ABCB1 gene polymorphism on tacrolimus CL/F were analysed.
Results: A two-compartment model adequately described tacrolimus pharmacokinetics. The CL/F was associated with weight (allometric scaling), but not age. Children with lower weight required higher TAC doses. CL/F was inversely associated with hematocrit ($p < 0.05$) and gamma glutamyl transpeptidase (γGT) levels ($p < 0.001$) and was increased by 45% in carriers of the CYP3A5*1 allele ($p < 0.001$). CL/F was not associated with concomitant medications. The median area-under the-concentration-time curve (AUC) was 97 h × ng/ml (range: 39–209). Tacrolimus concentrations measured 120 min after ingestion (C120) correlated better with AUC than the trough concentrations (C0) (Pearson $r^2 = 0.86$ and 0.78, respectively).
Conclusions: Children with lower weight and carriers of the CYP3A5*1 allele have a higher tacrolimus CL/F and therefore higher dose requirements.

BO215 A RANDOMISED-CONTROLLED TRIAL TO STUDY THE ADDITIVE VALUE OF CYP3A5 GENOTYPE-BASED TACROLIMUS DOSING IN LIVING-DONOR KIDNEY TRANSPLANTATION

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Background: The exposure to tacrolimus (Tac) is correlated with the expression and activity of the Tac-metabolizing enzyme CYP3A5. This isozyme is polymorphically expressed. Patients expressing CYP3A5 require a higher Tac dose to achieve therapeutic predose concentrations (C_0). The aim of this study was to evaluate whether dosing of Tac according to CYP3A5 genotype leads to earlier achievement of target Tac C_0 and consequently to a better clinical outcome.
Method: Recipients of a living-donor renal transplant ($n = 240$) were 1:1 randomly assigned to receive Tac at either a standard, fixed-dose (0.20 mg/kg per day) or based on the individuals' CYP3A5 genotype (0.15 mg/kg per day for non-expressers and 0.30 mg/kg per day for expressers). The primary endpoint was the proportion of patients within the target C_0 (10.0–15.0 ng/ml) at first steady-state (day 3 after transplantation). Secondary endpoints included the time required to reach the target C0 range, the number of dose modifications to reach the target C_0 and clinical outcomes during the first 3 months after transplantation.
Results: Three days after transplantation, 37.4% (95% CI: 28.5–47.0%) of the patients in the standard-dose (SD) group and 35.6% (95% CI: 27.0–45.0%) in the genotype-based (GB) group were within the target Tac C_0 range ($p = 0.79$). There was no significant between-group difference in the number of dose modifications needed to reach the target C_0 ($p = 0.30$). The time to achieve the targeted C_0 was also not significantly different: SD group 6 days (3–17 days) vs. GB group 6 days (3–28 days); $p = 0.36$. The clinical outcomes were similar in both groups.

Conclusion: Pharmacogenetic adaptation of the daily dose of Tac is not associated with earlier achievement of the Tac target exposure range and does not lead to improved clinical outcome.

BO216 PHARMACOGENOMIC INFLUENCE OF CYP3A5, CYP3A4*22 AND ABCB1 POLYMORPHISMS ON TACROLIMUS DOSE REQUIREMENTS AND TROUGH LEVELS IN SCOTTISH RENAL TRANSPLANT PATIENTS AND THE EFFECT ON CLINICAL OUTCOMES

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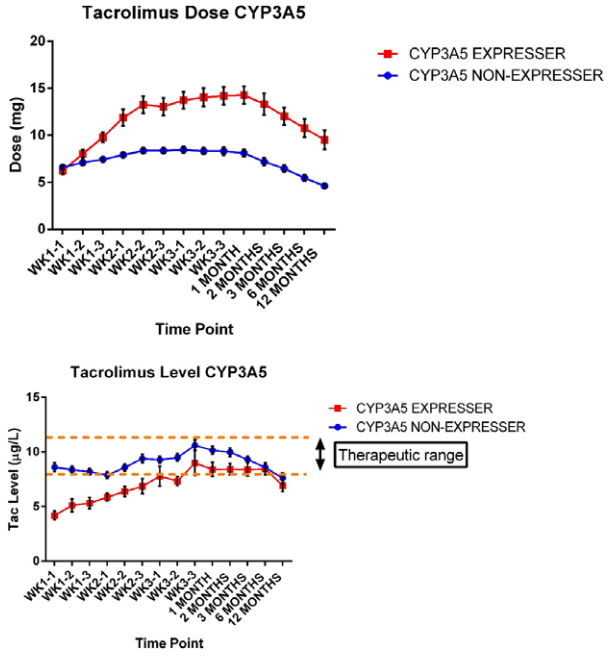
Introduction: Polymorphisms (SNPs) of CYP3A5, CYP3A4 and ABCB1 (P-gp) have been shown to influence tacrolimus pharmacokinetics in renal transplant patients. These SNPs have yet to be studied in a Scottish renal transplant population.
Methods: Between January 2008 and August 2012, 185 renal transplant recipients were included in the study where stored DNA and access to clinical records were available. DNA samples were genotyped for SNPs of ABCB1 exon 26 (3435C>T), CYP3A5 (6986A>G) and CYP3A4 intron 6 (CYP3A4*22) using a Taqman® drug metabolism genotyping assay and real-time PCR technique. Tac dose/trough levels were evaluated at 14 time points in the first 12 months and correlated with clinical outcome data (acute rejection, creatinine, graft and patient survival).
Results: 126 (68.1%) males and 59 (31.9%) females were in the study with a mean age of 47.20 ± 13.42 year. 149 (80.5%) patients did not express CYP3A5 (GG, *3/*3), 30 (16.2%) expressed one A allele (GA, *3/*1) and 6 (3.2%) two A alleles (AA, *1/*1). CYP3A5 expressers (GA/AA) were prescribed significantly higher doses of tacrolimus by the end of the 1st week post-transplant than non-expressers (*3/*3), 9.79 ± 2.96 mg vs. 7.44 ± 2.51 mg. ($p < 0.0001$). Trough tac levels were lower in CYP3A5 expressers immediately post-transplant (4.18 ± 2.46 μg/l) than the non-expressers (8.60 ± 4.94 μg/l), $p < 0.0001$ and at every time point up to 2 months. The dose-corrected Tac level (level/dose) was significantly lower post-transplant in CYP3A5 expressers (0.68 ± 0.39) compared with non-expressers (1.39 ± 0.82), $p < 0.0001$ and at every time point. ABCB1 and CYP3A4 SNPs did not significantly affect tacrolimus pharmacokinetics. Renal function, graft and patient survival and acute rejection were not influenced by the SNPs of any genotype.
Conclusion: CYP3A5 expression results in higher tac dose requirements, reduced tac levels immediately post transplant and reduced dose corrected tac levels. Clinical outcomes are not significantly affected.



BO217 COMPUTER-ASSISTED TACROLIMUS DOSING IMPROVE TARGET CONCENTRATION ACHIEVEMENT IN RENAL TRANSPLANT RECIPIENTS – A PROSPECTIVE RANDOMIZED STUDY

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Background: Achieving and maintaining target tacrolimus levels after renal transplantation is a challenge. Dose individualization utilizing a computer program combining a population pharmacokinetic model and Bayesian adaptive control may be helpful. The objective of this study was to prospectively evaluate the target concentration achievement of tacrolimus using computerized dosing compared with conventional dosing performed by experienced transplant physicians.
Methods: A single-center, prospective study was conducted. Eighty renal transplant recipients were randomized to receive either computerized (BestDose™) or conventional tacrolimus dosing during the first 8 weeks post-transplant. The median proportion of tacrolimus trough concentrations within the target range was compared between the groups. Standard risk (target 3–7 μg/l) and high-risk (8–12 μg/l) recipients were analyzed separately.
Results: Seventy-eight of the 80 included patients were randomized (Computerized dosing ($n = 39$): 32 standard risk/7 high-risk, Conventional dosing ($n = 39$): 35 standard risk/4 high-risk). A total of 1711 tacrolimus whole blood concentrations were evaluated. The proportion of concentrations per patient within the target range was significantly higher with computerized dosing. In standard risk patients a median of 90% [95% confidence interval (CI) 84–95%] was within the target range in the computer group vs. 78% [95% CI 76–82%] in the conventional group ($P < 0.001$). In high-risk patients the respective values were 77% [95% CI: 71–80%] vs. 59% [95% CI: 40–74%] $P = 0.04$).
Conclusions: Computerized dose individualization improves target concentration achievement of tacrolimus after renal transplantation. The computer software is applicable as a clinical dosing tool to optimize tacrolimus exposure and may potentially improve long-term outcome.

BO218 ELECTRONIC MONITORING FEEDBACK AND MOTIVATIONAL INTERVIEWING IMPROVES MEDICATION ADHERENCE IN HEART, LIVER AND LUNG TRANSPLANT PATIENTS: RESULTS FROM THE MAESTRO-TX RCT

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Background: Methodological shortcomings (e.g. small samples, vague intervention descriptions, use of unreliable adherence measures) prevent firm conclusions on efficacy of post-Tx medication adherence (MA) interventions. We tested if a 6 month intervention would improve post-Tx electronically monitored (EM) MA.
Methods: This RCT (run-in 3 months; randomization 1:1; 6 months intervention; 6 months follow-up), enrolled heart, liver and lung Tx, being >1 year post-Tx, in regular follow up at UZ Leuven, and on a twice daily tacrolimus-based regimen. Tacrolimus adherence was assessed using the Helping Hand®, an EM device for blister packages, in all patients over the entire study period. The usual care group talked to a researcher at each study visit during 20–30 min on an unrelated topic (attention bias prevention). Intervention patients received a multicomponent theory driven staged intervention during 3 contacts of 20–30 min over a 6 months period while using motivational interviewing, i.e. activation of the reminder and feedback functions of the Helping Hand, an education refreshment course, and feedback on the EM printouts. In case of non-adherence, reasons were assessed and tailored theory-based interventions proposed. GEE modeling was used to estimate the % of patients with correct dosing in each study arm (ITT analysis).
Results: 247 out of 274 patients agreed to participate (10% refusal), of which 205 were randomized (17% early drop-out). Before intervention, 82.6% of the intervention and 78.4% of the usual care group had correct dosing ($p = 0.2370$). Post-intervention, this % increased to 95.1% in the intervention vs. 79.1% in the usual care group (16% difference, $p < 0.001$). The intervention effect sustained during follow-up (97.8% vs. 78.6%; $p < 0.0001$).
Conclusion: Our intervention was efficacious to increase MA and was sustainable. Scalability of this intervention will depend on Tx clinics' willingness to integrate adherence measures and interventi.

BO219 A SYSTEMATIC REVIEW AND META-ANALYSIS OF DETERMINANTS AND OUTCOMES OF POST-TRANSPLANTATION MEDICATION NON-ADHERENCE IN ADULT SINGLE SOLID ORGAN TRANSPLANTATION

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Background: No systematic reviews/meta-analyses have examined both correlates and outcomes of immunosuppressive medication nonadherence (NA) in the adult transplant (Tx). Using the WHO framework, we investigated associations between post-Tx NA and demographic/socio-economic, patient-, treatment-, condition- and healthcare team/system-related correlates and clinical, economic and health-related quality of life outcomes in adults with lung, heart, liver and kidney organ Tx.
Methods: Using standard systematic review/meta-analysis methods (www.crd.york.ac.uk/PROSPERO), we conducted electronic searches of PubMed, CINAHL, PsycINFO, EMBASE through July 2012. Sixty-eight studies were identified/synthesized using the pooled odds ratio (OR) with 95% confidence interval (CI). Results

Socio-demographic correlates male gender (OR = 1.230; 95% CI = 1.063, 1.423), White ethnicity (OR = 0.735; 95% CI = 0.541, 0.997) social support (OR = 0.644; 95% CI = 0.468, 0.942) were significant-the latter two protective for NA. Patient-related factors higher sense of mastery/self-efficacy (OR = 0.435; 95% CI = 0.272, 0.696), higher self-care agency/ability (OR = 0.484; 95% CI = 0.440, 0.697), positive medication beliefs/attitudes (OR = 0.386; 95% CI = 0.230, 0.648), greater knowledge of diagnosis/treatment (OR = 0.602; 95% CI = 0.392, 0.927) were protective against NA; more side-effect symptom occurrence (OR = 1.559; 95% CI = 1.217, 1.998) was associated with higher NA. Treatment-related correlate time since Tx (OR = 1.461; 95% CI = 1.200, 1.779) significantly increased the odds of NA. Diabetes mellitus pre-Tx (OR = 0.670; 95% CI = 0.557, 0.807), a condition-related factor, was significantly protective for NA. Healthcare system-related factors were not explored due to insufficient studies. Late acute rejection (LAR) (OR = 2.356; 95% CI = 1.457, 3.809) was significantly associated with NA. Effect size heterogeneity found.
Conclusions: NA has multilevel correlates and a 2.36 times increased risk for LAR. Study heterogeneity shows future research opportunity.

BO220* A PROSPECTIVE RANDOMIZED TRIAL ON THE EFFECT OF USING AN ELECTRONIC MONITORING DRUG DISPENSARY DEVICE TO IMPROVE ADHERENCE AND NON-COMPLIANCE

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Background: The aim was to study the extent of non-compliance and the effect of using an electronic monitoring drug dispensary (EDD) device to improve adherence and non-compliance after kidney transplantation.
Material/Method: In a prospective randomized study 80 patients were allocated into two groups; A (n = 40) with EDD and B (n = 40) control group. EDD records the date and time when the patient picks up drugs from the dispenser. A reminder can be communicated with SMS, e-mail or phone in real time.

Patients were followed for 1 year with regards to missed medications and return visits to the outpatient clinic, emergency hospital admissions, biopsies, rejection episodes, kidney function, and concentration of drug in the blood. Multivariate regression was used for statistical testing.

Distribution between intervention group and control group

	Intervention group (N = 40)	Control group (N = 40)	Total
Living donor:	21 Patients	15 Patients	36 Patients
Deceased donor:	19 Patients	25 Patients	44 Patients
Sex:	15 women/25 men	13 women/27 men	28 women/52 men
Average age/years:	44.3 (9-68)	45.0 (2-69)	44.65 (2-69)
Screen failure:	1	0	1

Results: Compliance in the intervention group was 97.8%, with significant difference between weekdays (p = 0.033), most missed doses on Saturday and Thursday. Total number of missed doses of EDD was 524, predominantly in young adults and female (60%). Missed doses were twice as common in the evenings, ($p < 0.001$). The number of missed doses increased significantly over time (IRR = 1.23; 95% CI: 1.16–1.30). All study patients missed outpatient clinic visits 11 times. During the study period 92 biopsies were performed in 55 patients, 32 (17) in group A and 60 (38) in B. Biopsy-confirmed rejection episodes were three times more common in the control group, 13 patients in group B and 4 in A, (p = 0.054). Costs for rejection treatment was much higher in group B compared to A, €268 914 vs. €59 759, respectively. Average P-Creatinine at the end of the study period was slightly lower in the intervention group versus the control, 131/150 μmol/l. Tacrolimus through levels were equivalent between the groups, 7.32/7.22 ng/ml.

Conclusions: EDD is associated with high compliance. Patients in the EDD group had lower incidence of rejection episodes which may lead to better renal function and cost savings.

023 KIDNEY

BO221 THE RISK OF PREGNANCY-INDUCED ALLOIMMUNIZATION IN OFFSPRING TO MOTHER KIDNEY DONATION: LONG-TERM RESULTS

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Pregnancy-induced alloimmunization may provoke acute rejection episodes after kidney transplantation. We sought to determine the relative risk of rejection and graft loss of a child-to-mother compared to a child-to-father kidney transplantation.

Methods: We searched our database of 1696 adult living donor kidney transplants for child to parent combinations performed between1995-2013. We compared the incidence of biopsy proven acute antibody mediated rejection (AMR), acute cellular rejection (ACR) and chronic allograf nephropathy (CAN) in the two groups of child-to-mother (group1 = 29 cases) and child-to-father (group 2 = 38 cases). The two groups were compared also for graft and patient survivals.

Results: All patients were recipients of a first graft accept from 2 patients of group1 and one patient of group2 who underwent a second transplant. Four patients in group1 and three patients in group2 had positive CDC-PRA. Male recipients had higher incidence of diabetes (64.7% vs. 30.4%, p = 0.016). AMR occurred in 4 female recipients and none of the male recipients. There were two ACR and 3 CAN in the female group compared to 2 ACR and 1 CAN in the male group (ns). Thirteen grafts of group1 and seven grafts of group2 failed over a median follow up of 5.6 year. Graft survival for 1–5 and 10 years were 86.2%, 71.1% and 61.5% for female recipients and 97.2%, 82.1%, and 76.2% for male recipients (log rank test 0.07). Patient survival were 96.4%, 88.2% and 78.6% for female recipients and 97.4%, 86.4% and 86.0% for male recipients (ns).

Conclusions: Kidney donation of a child-to-mother seems to carry a higher risk for AMR and late graft loss compared to a child-to-father combination. With application of modern technique to identify low level allosensitization in female recipients and use of desensitization protocol these outcomes are expected to improve.

BO222* CD8 T CELL BIOMARKERS IMPROVES THE CAPACITIES OF THE KIDNEY TRANSPLANT FAILURE SCORE FOR THE LONG-TERM PROGNOSTIC OF KIDNEY GRAFT FAILURES

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Background: Beside the classical monitoring of kidney function using creatinemia or proteinuria, the assessment of other non invasive biomarkers have been proposed to early identify patients at-risk of kidney rejection. To reach a true clinical utility, the prognostic capacities of a biomarker has to be higher than other simple and available metrics such as clinical-based scoring system. We have previously shown that an increase in differentiated TEMRA CD8 T cells is associated with a 2-fold higher risk of kidney dysfunction. In this study, we evaluate if the monitoring of CD8-related biomarkers could improve the prognostic capacities of a clinical-based scoring system (Kidney Transplant Failure Score; KTFS).

Method: 161 kidney-transplant recipients have been prospectively enrolled and followed for more than 6 years (mean follow-up time 4.4 years; 6-year graft survival of 84.7%). At the end of the follow-up time, 14 patients returned to dialysis. Targeted analysis of CD8 T cell phenotypic markers have been performed on blood samples retrieved 1 year post-transplantation.

Results: High values of TEMRA, CD27-CD28- and GZMB+PERFD48- were associated with an increase in the risk of graft failure independently to the KTFS. The KTFS prognostic capacities of kidney graft failure could be improved by the inclusion of CD8-related biomarker with an increase of the area under the receiver-operator characteristic curve of 0.12 (95% CI 0.00 – 0.26; p = 0.0321). The composite scoring system allows a better classification of 26.1% of patients (NRI, 95% CI 3.2 – 49.8; p = 0.0321).

Conclusion: The combination of CD8-related biomarkers with clinical-parameters based KTFS allows to better predict patients at-risk of kidney graft failure and to target those with a more specific immunologic risk. Such score could be useful as decision tool in the clinical management of kidney transplant recipients.

023 KIDNEY

BO223 ROLE OF ANGIOTENSIN II TYPE I RECEPTOR ANTIBODIES IN TRANSPLANT GLOMERULOPHATHY IN KIDNEY TRANSPLANTATION: A SINGLE CENTRE ANALYSIS

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Background: Transplant glomerulophathy (TG) is an important cause of late graft loss in kidney transplant. The role of donor specific anti-human leukocytes antigen antibodies (DSA) in vascular rejection is well known but the significance of non-HLA antibodies is still unclear. These antibodies have polymorphic antigenic targets, including angiotensin type 1-receptor (AT1R-Ab). Their role in graft rejection, expecially in TG, is not yet established.
Methods: We retrospectively evaluated all patients (pts, $N = 50$) with a bioptic diagnosis of TG performed at Kidney Transplant Center in Turin, Italy (January 2008–December 2014). Serum samples were collected at the biopsy time, screened for DSA (Flow-PRA method, One Lambda) and for the presence of AT1R-Ab IgG (enzyme-linked immunosorbent assay, One Lambda). Detection range: >2.5 UI/ml; positive value set >17 UI/ml, at risk 10–17 UI/ml, negative <10 UI/ml.
Results: Pts were divided as follows: 41/50 (82%) AT1R-Ab negative; 6/50 (12%) at risk; 3/50 (6%) positive. Groups characteristics detailed in table 1. No significant differences comparing the group with AT1R-Ab and the negative one for the positivity of DSA. DSA were present in: 2/3 AT1R-Ab positive pts, 4/6 at risk pts, 28/41 negative pts. Graft survival was not conditioned by the presence of AT1R-Ab, p = NS.
Conclusions: The detection of non-HLA antibodies is becoming important in antibody-mediated rejection. In our TG population the presence of AT1R-Ab appeared poorly represented. The positivity for these antibodies was independent from the presence of DSA and didn't correlate with a different graft survival.

BO224 BASILIXIMAB IN KIDNEY TRANSPLANTATION ACCORDING TO IMMUNOLOGIC RISK

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Background: The optimal immunosuppressive induction therapy in kidney transplant recipients at low immunologic risk of early acute rejection (AR) is still controversial. The use of Basiliximab (Basx) in immunosuppressive induction therapy has led to a significant decrease of AR and due to its low adverse effects, Basx has been used more frequently than Thimoglobulin (rATG) in these patients.
Objective: To evaluate risk predictor factors of early AR in patients at low immunologic risk subjected to immunosuppressive induction therapy with Basx, calcineurin inhibitor (CNI) micofenolate mofetil (MMF) and prednisolone (PN).
Methods: We performed a review of patients at low immunologic risk (panel reactive antibody (PRA) < 50%, who had undergone a first deceased-donor transplant) and subjected to immunosuppressive induction therapy with Basx, CNI, MMF and PN ($n = 346$). Early AR was defined as any rejection occurring until 12 months post-transplant. Risk predictor factors of AR were evaluated by logistic regression and to find the best cut-off of PRA related to a higher incidence of AR, was performed the receiver operating characteristic analysis (ROC curve).
Results: The rate of AR was 7.8%. Risk predictor factors for AR were associated to age at the time of transplantation (p value = 0.030) and to the PRA level (p value = 0.001), through multivariate logistic regression analysis. ROC curve analysis (area 0.628; p value = 0.042; 95%CI 0.49–0.74) confirmed that PRA>10% was related to an increased incidence of AR (19.2% vs. 6.0%, p value = 0.005) displaying a relative risk (RR) of AR of 3.2 (95%CI 1.52–6.65).
Conclusions: A higher incidence of early AR was observed in kidney transplant patients at low immunologic risk and PRA >10%. This result supports the selection of patients with PRA>10% to be considered at an increased level of immunologic risk and the use of rATG as immunosuppressive induction therapy in these cases.

	AT1R-Ab positive	AT1R-Ab negative	AT1R-Ab at risk	p-value
Male, *n* (%)	3/3 (100)	20/41 (48.8)	4/6 (66.7)	0.18
Age (years, ds)	55.8 ± 14.6	55.2 ± 12.9	47.9 ± 16.2	0.5
Cause of renal failure: immunological, *n* (%)	1/3 (33.3)	14/41 (34.1)	2/6 (33.3)	0.5
Cause of renal failure: not immunological, *n* (%)	2/3 (66.6)	12/41 (29.2)	3/6 (50)	0.5
Cause of renal failure: unknown, *n* (%)	0	15/41 (36)	1/6 (16.7)	0.5
PRA >20%, *n* (%)	0	8/41 (25.8)	3/6 (75)	0.2
C4d positivity	1/3 (33.3)	17/41 (41.5)	3/6 (50)	0.8
Preeclampsia, *n* (%)	0	3/41 (7.3)	0	0.7
Vasculopathy pre-transplant, *n* (%)	0	10/41 (25)	3/6 (50)	0.25
Vasculopathy post-transplant, *n* (%)	0	11/41 (28.2)	2/6 (33.3)	0.5
Cardiopathy pre-transplant, *n* (%)	1/3 (33.3)	3/41 (7.9)	1/6 (16.7)	0.34
Cardiopathy post-transplant, *n* (%)	1/3 (33.3)	3/41 (7.9)	2/6 (33.3)	0.12

BO225 PHENOTYPE OF VASCULAR REJECTION AFTER KIDNEY TRANSPLANTATION: A HIDDEN THREAT

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Introduction and aims: Acute vascular rejection (AVR) is a severe clinical condition with detrimental impact on kidney allograft survival. Although it has been thought to be T-cell mediated process, recent clinical findings showed its association with donor specific alloantibodies and resistance to usual, against T-cells directed treatment. Therefore, correct assessment of AVR phenotype would be beneficial for adaptation of treatment strategy and improving long-term prognoses of kidney allografts.
Methods: We retrospectively analysed 206 patients who underwent a kidney transplantation in year 2012. AVR was defined as a presence of intimal arteritis (v) in biopsies within 1 year after transplantation. "Isolated v-lesion" formed a subgroup of AVR and was characterized as an intimal arteritis with minimal interstitial inflammation and tubulitis (v1–3, i ≤ 1, t ≤ 1, C4d negat,, ptc negat., g negat.).
Results: AVR was found in 23/206 patients (11%) and represented 48% of all rejection findings within 1 year after Tx. In most cases (21/23, 91%) AVR was found in indication biopsies, only 2 cases were diagnosed from protocol biopsy and marked as subclinical. In 74% cases was AVR classified as pure acute T-cell mediated rejection. Conventional steroid treatment was applied in 48% patients, from which 55% cases were steroid-resistant. If rATG or AMR targeted therapy was used as initial treatment, v-lesions resolved in 75% and 84% patients, respectively. Luminex was evaluated in 52% of AVR and confirmed to be positive in 75% of all evaluated cases. Chronic rejection developed in 4 cases, in 2 cases as a consequence of acute AMR and in other 2 cases as a result of steroid-resistant "isolated v-lesion".
Conclusions: Vascular lesion is a frequent finding in the 1st year after renal transplantation and is associated with severe clinical course. Innovative diagnostic and therapeutic algorithms are essential to mitigate the impact of this rejection phenotype on transplanted kidney.

BO226 TH-17 ALLOIMUNE RESPONSES IN RENAL ALLOGRAFT BIOPSIES FROM RECIPIENTS OF KIDNEY TRANSPLANTS USING EXTENDED CRITERIA DONORS DURING ACUTE T-CELL-MEDIATED REJECTION

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Although renal transplantation using expanded criteria donors has become a common practice, immune responses related to immunosenescence in those kidney allografts have not been studied yet in humans. We performed a retrospective molecular analysis of the T cell immune response in 43 kidney biopsies from patients with acute T-cell mediated rejection including 25 from recipients engrafted with a kidney from expanded criteria donor and 18 from recipients grafted with optimal kidney allograft. The clinical, transplant and acute T-cell mediated rejection characteristics of both groups were similar at baseline. The expression of RORgt, Il-17 and T-bet mRNA was significantly higher in the elderly than in the optimal group ($p = 0.02$, $p = 0.036$ and $p = 0.01$, respectively). Foxp3 mRNA levels were significantly higher in elderly patients experiencing successful acute T-cell mediated rejection reversal ($p = 0.03$). The presence of IL-17 mRNA was strongly associated with non-successful reversal in elderly patients ($p = 0.008$). Patients with mRNA IL17 expression detection and low mRNA Foxp3 expression experiencing significantly more treatment failure (87.5%) than patients with no mRNA IL17 expression and/or high mRNA Foxp3 (26.7%; $p = 0.017$). Our study suggests that Th17 pathway is involved in pathogenesis and prognosis of acute T-cell mediated rejection in recipients of expanded criteria allograft.

BO227 EXPRESSION OF A COMPLEMENT REGULATORY FACTORS IN RENAL ALLOGRAFTS DURING ACUTE T-CELL-MEDIATED REJECTION

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Background: Locally produced C3 from allografts during acute T-cell-mediated rejection (ATCMR) have been the focus of recent research interest. The regulation of local complement production may provide prognostic information related to the condition of a graft. We examined the expression of a membrane cofactor protein (MCP), a complement regulatory protein, produced by rejecting renal allografts, and followed the clinical prognosis of the graft. Methods/Materials

We used 64 human renal transplant biopsies for the immunohistocemical staining of MCP and complement after the diagnosis of ATCMR type I and type II. The expression of MCP was then examined for the functional outcome of the graft and clinicopathological correlations.
Results: C3c deposition in renal tubular cells was observed in 60 patients (93.8%). The high expression of MCP by tubular cells of the graft were consistent with lower creatinine levels at 2 and 12 month after antirejection treatment, compared with a low MCP expression. 5-year graft survival was better in patients with a high MCP expression compared to those with a low MCP expression, 100% vs. 76.6% respectively. The age of the donors in the high MCP expression group was significantly lower than that of the low MCP expression group.
Conclusion: The findings herein indicate that MCP expression in renal tubular cells of a graft during ATCMR could be an indicator for treatment and graft survival.

BO228* BORTEZOMIB IN THE TREATMENT OF RESISTANT ACUTE ANTIBODY- MEDIATED REJECTION: A SINGLE CENTRE EXPERIENCE

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Introduction and Aims: The aim of this retrospective single centre study was to analyse efficacy and safety of plasmapheresis (PP)/intravenous immunoglobulins (IVIG) versus bortezomib (B) based treatment regimen in antibody mediated rejection (AMR).
Method: Medical records of 670 patients that had undergone kidney transplantation between 1/2012–7/2014 were analyzed. AMR was defined as a C4d+ staining along with positive donor specific antibody (DSA) that occurred early after transplantation. In the group one AMR was treated using 5 cycles of PP followed by IVIG 0.2 g/kg ($n = 15$). The second group were patients with positive CDC a FXCS after treatment ($n = 17$), these patients received B [1 cycle of 4 doses of B (1.3 mg/m2)], PP and a dose of Rituximab (375 mg/m2). Resistant AMR was defined as a persisting deterioration or non-function of renal allograft in patients with histological verification of AMR, positive C4d+ staining and detection of DSA receiving standard antirejection treatment with PP + IVIG. Patients (pts) were followed for 3–12 months.
Results: AMR was diagnosed in 32 out of patients (4.7%) and occurred at 12 POD. There were not a difference between graft and patient survival in B group and in PF+ IVIG group. There were no significant differences in panel reactive antibodies, HLA mismatches, length of dialysis therapy. The number of retransplantation were significant higher in B group ($p = 0.005$). Based on therapeutic effect, 11 pts received 1 cycle, 4 pts received 2 cycles and 2 patient was treated by 3 cycles of therapy. The side- effects observed were leucopenia (59%), thrombocytopenia (82%), fluid retention (29%), polyneuropathy (29%). Using IVIG + PP versus B regimes in treating acute AMR led to decrease in DSA. In both therapeutical regimes we observed significant improving of renal function- PP+ IVIG (S-Cr, $p = 0.001$), B regime (S-Cr, $p = 0.0003$).
Conclusions: Combination of PP and B with Rituximab is an effective approach to DSA decrease in cases of resistant

BO229* BORTEZOMIB TREATMENT IN ANTIBODY MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Several studies demonstrated bortezomib therapy for antibody-mediated rejection (AMR) in renal transplants. However, the treatment efficacy according to target antigen or occurrence time of AMR has not been identified.

We describe our experience with bortezomib used to treat AMR in ten renal transplant patients.
Methods: Ten patients who received bortezomib for treatment pure AMR were included in this study. All patients were treated and did not respond to conventional treatment composed of plasmapheresis with intravenous immunoglobulin + rituximab. Patients received one to two cycles of bortezomib (4×1.3 mg/m^2 per cycle). Early AMR was defined as occurring within 6 months post-transplant.
Results: A total of eleven episodes were treated with bortezomib (6 early and 5 late). One patient had anti-ABO antibody with anti-HLA antibody. Another patient had no anti-HLA antibody, but had a high titer of anti-angiotensin II type 1 receptor antibodies. All episodes of early onset AMR were fully recovered after 1 cycle of bortezomib treatment regardless of target antigen. Three of five late onset AMR episodes responded to bortezomib. Overall, there was a significant improvement in mean estimated glomerular filtration rate at the end of therapy as compared to the eGFR at the time of diagnosis ($p = 0.005$). Bortezomib related toxicities (thrombocytopenia and peripheral neuropathy) were all transient and recovered with conservative management.
Conclusion: Bortezomib is an effective treatment for refractory AMR regardless of target antigen.

Table 1. Changes of allograft function and antibodies after bortezomib treatment

Patient	At AMR diagnosis				Bortezomib	At 3 months aft	
	Antibodies	C1q	Cr	eGFR	Cycle	Antibodies	
A	A2(14589), B13(1365)	N/A	4.87	11	1st cycle	DSHA(-)	4
	A2 (6738), DR12(1571)	(+)	3.06	18	2nd cycle	N/A	1
B	Anti-B IgM/IgG(1:64/1:256) DR8(16389)	N/A	5.63	8	1	Anti-B IgM/IgG(1:16/1:64) DSHA(-)	0
C	B52(1063), DR15(12466)	N/A	4.47	11	1	A30(1068), DR15(7809)	1
D	B27(12878), DQ9(17209)	(+)	2.31	36	1	DQ9(11404)	1
E	B51(4136)	(-)	2.32	29	1	B51(2182)	1
F	DSHA(-), AT1R Ab > 50	N/A	8.52	7	1	N/A	2
G	DR13(14274), DQ6(5148)	(-)	4.26	11	2	DR13(8943), DQ6(1306)	4
H	DR7(2118), DQ2(17258)	(+)	3.37	20	2	DR7(2109), DQ2(21065)	2
I	DSHA(-), Donor CREG Ab-DR13(11372)	(-)	2.22	23	2	Donor CREG Ab-DR13 (17475)	1
J	B13(9177)	(-)	3.7	13	1	B13(2583), DQ5(3338)	3

AMR=antibody-mediated rejection, Cr=creatinine, eGFR=estimated glomerular filtration rate(MDRD), DSHA=donor specific anti-H

BO230 HIGH REJECTION RATES AFTER KIDNEY TRANSPLANTATION WITH LOW IMMUNOLOGICAL RISK: ARE THE KDIGO GUIDELINES FOR EVERYBODY?

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Introduction: The KDIGO guidelines recommend IL-2 RA as induction therapy for patients in low immunological risk and a lymphocyte-depleting agent for patients at high immunological risk. Our aim was to compare both therapies in a Colombian population as well as to identify immunological risk factors.
Methods: From 1/2011 to 6/2013 we performed 39 kidney transplantations. We evaluated demographic data, immunological risk, induction therapy, HLA mismatch (MM), PRA and cold ischemia time. We analyzed the outcomes and immunological patrons at 1-year follow up.
Results: Our collective was 36 ± 15 year-old, with 51% males, 82% Hispanic and 18% Afrocolombian. Three patients (PRA<20%) did not receive induction. From the rest, 13 patients with high immunological risk (PRA20%; Afrocolombian race; expanded criteria donor) received ATG (Thymoglobuline©, Sanofi-Aventis, France) and 23 patients (low risk; PRA<20%) received Basiliximab (Simulect©, Novartis Pharma, Switzerland). Acute cellular rejection was higher in patients without induction (66% vs. 13%; p: <0.02). The 30-day acute rejection rate was higher in patients who received Basiliximab, in spite of lower immunological risk, compared with patients at high risk, who received ATG (17.4% vs. 7.6%; $p < 0.05$). No differences regarding acute rejection at follow-up were found. However, in patients with MM 4–6, ATG showed a lower acute rejection. No humoral rejection episodes were observed at 1-year follow up. Renal function was good (Creatinine: 1.2 mg/dl). Graft and patients survival was 97.4%.
Discussion: Acute cellular rejection in patients without induction is higher than in patients with induction, confirming KDIGO guidelines. Induction with Thymoglobuline showed fewer acute rejection episodes in our population despite higher immunological risk. The high acute rejection rate in patients treated with Basiliximab and high MM (4–6) suggests that Thymoglobuline could be a good option in this apparently low-risk population.

BO231 THE REMISSION OF RENAL INJURY IN TACROLIMUS TO SIROLIMUS CONVERSION RENAL TRANSPLANT RECIPIENTS IS DEPENDENT ON THE INHIBITON OF CYTOKINE- CHEMOKINES SIGNALING

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Background: Conversion from tacrolimus to sirolimus-based immunosuppression is associated with improved renal function and stabilization of renal-allograft lesions. Cytokine and chemokines play an important role in renal-allograft lesions. When stimulated with proinflammatory cytokines, endothelial and parenchymal cells in the kidney produce chemokines that are necessary for the initial migration of leukocytes into the renal allograft. Subsequently, the renal injury after transplantation ocurred.
Methods: We included 48 recipients who received a first renal graft in West China Hospital. Among all the renal transplant recipients, 24 recipients received a tacrolimus (TAC) based regimen, the other 24 recipients received a sirolimus (SRL) based regimen which conversion from tacrolimus. Plasma cytokine IL-1β, IFN-γ, IL-17, IL-6, IL-10 and Chemokines IP-10, MCP-1, MIP-1b, IL-8 were measured using the Bio-Plex® suspension array system which utilizes Luminex® xMAP™ multiplex technology.
Results: After conversion to SRL for more than one month, the renal function has turned better for those recipients. For the cytokine and chemokines analysis,IL-6, IL-1β and IL-17 were positive correlation with MIP-1b and IL-8 ($p < 0.05$), we found that Th1 related cytokine (IL-1β and IFN-r) and Th17 related cytokine (IL-17, IL-6) decreased significantly in the recipients used SRL based regimen compared with tacrolimus group ($p < 0.05$). On the other hand, we found the plasma concentrations of MCP-1 and MIP-1b in SRL group decreased significantly when compared with TAC group ($p < 0.05$).
Conclusions: In summary, we conclude that conversion from CNIs to sirolimus in kidney-transplant recipients is associated with improved renal function. Those proinflammatory Cytokine and chemokines play an important role for tacrolimus treated recipients in mediating the inflammatory process of renal nephrotoxicity formation.

BO232* STEROID FREE IMMUNOSUPPRESSION IS POSSIBLE AND FEASIBLE ALSO LATE AFTER KIDNEY TRANSPLANTATION (KTX)

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Background: Guidelines quote that steroid withdrawal months after kidney transplantation imposes a higher risk of rejection and worse long term results. We could not reproduce these findings in our population and therefore retrospectively compared our long-term results of patients who received a maintenance therapy with steroid-continuation (SC) with patients who got steroids withdrawn 12–18 months after KTX (SWD).
Methods: 2×216 patients were matched for age, sex, transplant date, no. of transplants and soured of donation out of a cohort of 809 pts transplanted between 1984 and 2012. 60% were male, mean age 49 yrs, 10% living donations, mean waiting time 56 months. 65% received induction therapy, 51% CsA compared to 44% tacrolimus, 66% MMF.
Results: Patient survival was comparable, graft survival after 5, 10 and 20 yrs significantly better after steroid withdrawal (92 vs. 80%, 73 vs. 55%, 31 vs. 25%, $p = 0.001$). Death-censored graft survival was also improved compared to SCG-patients. There was a trend for more biopsy proven rejections in SC-patients, however low grade cellular rejections (Banff borderline/°I) were numerically increased in SWD. Typical steroid-related side effects, e.g. new onset diabetes after transplantation (18 vs. 25%), major adverse cardiovascular events (13 vs. 17%) or fractures (2.3 vs. 5.6%) occurred numerically less frequent after SWD, due to rather low incidences differences were not significant. Incidences of CMV-infection or malignancy were not related to steroid continuation.
Conclusion: Steroid withdrawal also months after KTX results in significantly better graft survival without a relevant increase in acute rejection episodes and with trends for reduced typical complications of steroid application. However this should be conducted under the auspices of induction therapy and tailored immunosupression. Adding DSA-analysis may even improve selection of appropriate patients. Selection bias may potentially impact these results.

BO233 COMPARISON OF EFFECTS OF INDUCTION THERAPY WITH ALEMTUZUMAB VERSUS ANTITHYMOCYTE GLOBULIN AMONG HIGHLY SENSITIZED KIDNEY TRANSPLANT CANDIDATE

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Objective: We compare induction therapy utilizing alemtuzumab versus antithymocyteglobulin in high risk kidney transplant patient populations at Nemazee hospital (Shiraz, Iran).
Methods & Materials: Two hundred and fifty-one patients underwent kidney transplantation between 2009 and 2012. We preformed this retrospective study after reviewing the transplant database of all high risk kidney transplant recipients. Inclusion criteria were age between 18–68 years, recipients of more than two times kidney transplantation, and more than 30% panel-reactive antibody. We compared outcomes of induction therapy with alemtuzumab and antithymocyteglobulin among kidney transplant recipients. Data collection form was consisted of demographic information, drug intake details, underlying disease, and early complications.
Results: One hundred thirty high risk kidney transplant candidate were included in our study. Fifty eight (44.6%) patients received induction with alemtuzumab and 72 (55.4%) with antithymocyteglobulin. There were 3 graft failures in the alemtuzumab group and 8 failures in the ATG group due to rejection episodes. Acute cellular rejection episodes were observed in 5 patients in alemtuzumab group and 19 patients in ATG group. There was statistical significance of the acute rejection incidence between groups ($p = 0.009$). Delayed graft function developed in 11 patients receiving alemtuzumab, against the 27 patients who receiving ATG. Delayed graft function developed in 11 patients receiving alemtuzumab, against the 27 patients receiving ATG. We found a significant difference regarding delayed graft function between two groups. ($p = 0.021$).
Conclusion: We found a significant difference between two groups, in acute rejection and delayed graft function.

BO234 EVEROLIMUS DE NOVO WITH REDUCED-EXPOSURE CYCLOSPORINE IN RENAL TRANSPLANT RECIPIENTS AT HIGH RISK OF EFFICACY FAILURE: RESULTS OF A *POST-HOC* ANALYSIS

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Purpose: Scarce data exist on the efficacy of *de novo* everolimus (EVR) with reduced calcineurin inhibitor (rCNI; cyclosporine A [CsA]) in renal transplant recipients (RTxR) with known risk factors for graft rejection. Here, we present a *post-hoc* analysis assessing efficacy outcomes in subpopulations of RTxR at high risk for efficacy failure receiving EVR with rCsA or mycophenolic acid (MPA) plus standard (s) CsA.
Methods: A2309 (NCT00251004), a 24-month (M), multicentre, open-label study randomised 833 RTxR to EVR (C0 3–8 or 6–12 ng/ml)+rCsA, or MPA+sCsA; all with basiliximab induction ± steroids. Composite efficacy endpoint (treated biopsy-proven acute rejection (tBPAR), graft loss, death or loss to follow-up) and evolution of renal function (eGFR; MDRD4) were assessed at M12 and M24. The subpopulations identified to be at high risk of efficacy failure (Cox proportional hazard modelling findings: male gender, younger recipient age, African-American race, delayed graft function [DGF], HLA mismatch ≥3 and increasing donor age) were evaluated.
Results: Similar incidence of composite endpoint was seen across subpopulations at M24 (Table 1a). Incidence of tBPAR was similar for EVR 3–8 ng/ml and MPA in all subpopulations. In the HLA mismatch ≥3 subpopulation, tBPAR was less frequent with EVR 6–12 ng/ml vs. MPA ($p = 0.049$). In patients with DGF receiving EVR 3–8 ng/ml, mean eGFR (SD) was numerically higher versus MPA (51.0 [20.8] vs. 40.3 [20.3] ml/min/1.73 m^2). CsA exposure was reduced by 53–75% and 46–75% in EVR 3–8 and 6–12 ng/ml arms, respectively, versus MPA arm. Safety was comparable between EVR and MPA groups across subpopulations (Table 1b).
Conclusion: These findings suggest that reduction in CsA exposure in *de novo* EVR+rCsA offers immunosuppressive efficacy and overall safety in RTxR at increased risk for efficacy failure, at M24. Higher eGFR was seen in patients with DGF receiving EVR 3–8 ng/ml.

Table 1: Incidence of a) composite efficacy endpoint[a]; b) AEs and SAEs

Subpopulation	EVR 3–8ng/mL n/N (%)	EVR 6–12ng/mL n/N (%)	MPA n/N (%)
a) Composite efficacy endpoint[a] at M24 post-transplant in high risk subpopulations (ITT population)			
Male gender	64/177 (36.2)	50/191 (26.2)	61/189 (32.3)
Recipient age <50 years	61/157 (38.9)	44/153 (28.8)	41/143 (28.7)
Black race	14/35 (40.0)	15/40 (37.5)	16/39 (41.0)
Delayed graft function	13/27 (48.1)	17/30 (56.7)	14/26 (53.8)
HLA mismatch ≥3	73/210 (34.8)	50/194 (25.8)	62/202 (30.7)
Donor age ≥50 years	37/95 (38.9)	21/76 (27.6)	26/94 (27.7)
b) AEs and SAEs by M24 post-transplant (Safety population)			
AEs (between groups)	99.3%	99.3%	98.9%
SAEs (between groups)	64.2%	69.4%	61.5%
SAEs in high risk subpopulations			
Male gender	114/175 (65.1)	120/190 (63.2)	115/188 (61.2)
Recipient age <50 years	98/155 (63.2)	97/152 (63.8)	79/140 (56.4)
Black race	18/32 (56.3)	23/40 (57.5)	26/37 (70.3)
Delayed graft function	18/27 (66.7)	23/29 (79.3)	22/25 (88.0)
HLA mismatch ≥3	131/208 (63.0)	131/193 (67.9)	123/199 (61.8)
Donor age ≥50 years	64/94 (68.1)	56/76 (73.7)	62/93 (66.7)

[a]Treated biopsy-proven acute rejection, graft loss, death or loss to follow-up
AEs, adverse events; EVR, everolimus; HLA, human leukocyte antigen; ITT, intent-to-treat; M, month; MPA, mycophenolic acid; SAEs, serious adverse events
Statistical comparisons of EVR 3–8ng/mL and EVR 6–12ng/mL vs MPA were all non-significant

BO235 THROMBOSPONDIN-1 INDUCES EXPRESSION OF REGULATORY LYMPHOCYTES IN KIDNEY TRANSPLANT PATIENTS TREATED WITH MTOR INHIBITORS

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Introduction and aims: Regulatory lymphocites (Ly) B and T (Breg and Treg) are key mediators of kidney transplant (KT) immunological tollerance. Trombospondin-1 (TSP) is a matrix protein with immunoregulatory activity that may be released by several cell types as soluble factor. In this study we investigated if immunosuppressive treatment in KT may influence Ly phenotype and if TSP is involved in this process.
Methods: We enrolled 60 patients with stable graft function, 20 trated with Tacrolimus (TAC), 20 sirolimus (SRL), 20 everolimus (EVE). In patients blood Ly were characterized by FACS analysis and TSP measured by ELISA. *In vitro* Ly and kidney tubular cells (KTC) were cultured with TAC, EVE or SRL; TSP pathway was analyzed.
Results: Patients treated with SRL or EVE had increased levels of Treg, Breg and TSP if compared with TAC ($p < 0.05$), no differences were found in memory Ly. The highest T and B reg levels were found in EVE group. TSP correlate with Treg levels ($r2 = 0.35$). *In vitro*, SRL and EVE but not TAC induced increased expression of TSP in B and T-Ly as in KTC ($p < 0.05$). Increasing doses of TSP induced regulatory phenotype in B and T cells as did supernatants of KTC stimulated with SRL or EVE. All these effects were knocked-down by inhibiting TSP syntesis (with RNA silencing) or activity (with competitive antibody for TSP receptor CD47).
Conclusion: TSP is produced by Ly and KTC and influenced B and Treg phenotype by an endocrine activity. TSP syntesis seems to be increased by mTOR inhibitors (SRL and EVE) but not TAC; this finding may partially explain the role of mTOR in transplant tollerance induction.

BO236 EFFECT OF EARLY CONVERSION TO EVEROLIMUS ON CARDIOVASCULAR PARAMETERS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: RESULTS FROM THE ELEVATE STUDY

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Background: Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality post kidney transplantation (KTx). Long-term exposure to calcineurin inhibitors (CNIs) contributes to an increased CVD risk. The ELEVATE study (NCT01114529) compared an early switch from a CNI to

everolimus (EVR)-based regimen with continued CNI in *de novo* KTx recipients (KTxR). We present here the 12-month (M) data on CV parameters.
Methods: In this 24M, multicentre, open-label study, KTxR were randomised (RND) after 10–14 weeks to EVR (C0 6–10 g/ml) or continued standard CNI (C0, tacrolimus: 5–10 ng/ml, cyclosporine: 100–250 ng/ml); all receiving enteric-coated mycophenolate sodium and steroids. Change in arterial pulse wave velocity (PWV; by pulse wave blood monitoring) from RND to M12 and 24-h blood pressure (BP) monitoring was done. Patients having both RND and M12 LVMi values were included in this analysis.
Results: At RND, mean PWV (m/s) was 7.81 and 7.64 for EVR (n = 94) and CNI (n = 123), respectively, and changed to 7.55 for EVR (n = 84) and 7.73 for CNI (n = 115) at M12. For patients with left ventricular hypertrophy (LVH), mean PWV was assessed in 47 EVR (40.42% concentric, 59.58% eccentric) and 68 CNI (48.53% concentric, 51.47% eccentric) patients at RND, and in 40 EVR (40% concentric, 60% eccentric) and 63 CNI (46.03% concentric, 53.97% eccentric) patients at M12; the difference between mean PWV (m/s) was −0.33 in EVR and +0.12 in CNI groups. Stratification by concentric and eccentric LVH showed greater change in PWV in EVR versus CNI groups for concentric LVH (difference: −1.07 vs. +0.35); marginal changes were observed for eccentric LVH (difference: +0.14 vs. −0.07). No significant difference was noted in systolic and diastolic BP between the groups. Currently, M24 analyses are ongoing.
Conclusion: Early conversion to everolimus showed a trend for improved vascular flexibility compared to standard CNI. BP did not show changes between the groups.

BO237 LOW PREVALENCE OF POST-TRANSPLANT ANTI-HLA CLASS 2 ANTIBODIES IN LIVING DONOR KIDNEY RECIPIENTS TREATED WITH ANTI-THYMOCYTE GLOBULIN (ATG) INDUCTION THERAPY- SINGLE CENTER EXPIRIANCE

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Background: The mono or policlonal antibodies (Ab) induction therapy (th) as a standard treatment after solid organ transplantation, might have long term effect on production of anti –HLA Ab. The aim of our cross-sectional study is to investigate the prevalence of anti- HLA Class 1 and 2 ab in living donor kidney recipients treated with different induction th (ATG or Basiliximab).
Methods: The serum samples from 46 stable recipients 61 months after the surgery (range 12 to150) were investigated using a single antigen Luminex assay. Mean fluorescence intensity (MFI) more then 800 has taken as a relevant amount of ab. All patients were under standard immunosuppression and induction th (ATG or Basiliximab) and triple drug maintenance th (Tacrolimus or Cyclosporine, MMF and steroids). The CDC cross match was negative in all patients. Transplantation was performed from related n = 38 and non-related (spousal) n = 7 donors with minimum 1 HLA compatibility. The pts were divided in ATG group (Gr. 1) and Basiliximab group (Gr. 2). The groups was match regarding recipient's age, gender, primary renal diseases and the average time of follow up.
Results: A relevant amount of anti-HLA Class 2 ab were detected in 13 recipients, in ATG group (15%) and 10 in SIM group (38%) with an average MFI of 980 compared versus 4630, respectively ($p < 0.01$). Regarding anti-HLA class 1 ab the differences was not significant. The most frequent anti-HLA ab identified were against A1, A2, A3, A68, B44, B45, DR18, DR7, DR17, DQ 7, DQ8 and DQ9. Pts in Gr. 1 showed significantly less proteinuria than pts. in Gr. 2 (0.44 vs.0.75 gr/24 h, respectively). There was no significant difference in serum creatinin, GFR, rejection episodes and donor specific ab.
Conclusion: There is a positive role of ATG induction th on prevalence of anti HLA-Class 2 ab which could be of importance for long term graft and patients survival. More careful investigation including protocol biopsies are needed for more relevant resuts.

BO238 BENEFICIAL EFFECT OF INTRAVENOUS IMMUNOGLOBULINS IN PATIENTS LOWLY SENSITIZED

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Allograft nephrectomy is a major risk factor for anti-HLA sensitization, which is likely to both increase time on the waiting-lists and decrease further allograft survival. There have been no studies of how to prevent such sensitization.

Ten patients without DSA were treated with 1.5 g/kg of intravenous immunoglobulins (IVIG) at the time of nephrectomy between January 2011 and January 2013. Control historical group included 13 patients without any DSA and not treated with IVIG. Anti-HLA antibodies (Luminex assays) were assessed at baseline, and 3 months after nephrectomy.

Anti-HLA sensitization at baseline was similar in both groups. In patients without any DSA treated with IVIG, DSA sensitization did not increase three months after allograft nephrectomy . Number of class I and class II DSA were 1 (0–2) and 0 (0–1) respectively three months after surgery ($p = 0.50$ and $p = 0.06$ respectively compared to baseline). Considering non-DSA sensitization, number of class I increased significantly in IVIG treated patients (5 (2–20) vs. 1 (0–4.25) at baseline; $p = 0.03$) but number of class II non DSA antibodies was stable (1 (0–9.5) vs. 0 (0–3.25) at baseline; $p = 0.58$). In historical group, all DSA and non DSA parameters studied increased significantly significantly three months after nephrectomy.

Our observations suggest that high doses of IVIG can minimize sensitization after allograft nephrectomy in patients without DSA at the time of surgery.

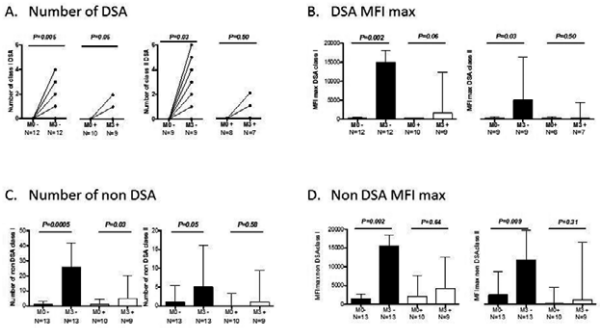

Figure 1 : Progression of anti-HLA sensitization 3 months after allograft nephrectomy

BO239 LATE CONVERSION TO EVEROLIMUS WITH MINIMIZATION OF CALCINEURIN INHIBITORS CONSISTENTLY RECOVERS KIDNEY GRAFT FUNCTION WITHOUT ACUTE REJECTION

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Introduction: Although kidney graft survival within 5 years after transplantation is now achieved in more than 95% of recipients, chronic graft deterioration remains a factor limiting long-term survival. Chronic nephrotoxicity caused by calcineurin inhibitor (CNI) is one of the major causes of chronic graft injury, thus minimization of CNIs by administration of everolimus (EVR), is expected to relieve their toxic effects. The aim of this study was to evaluate late conversion of EVR on CNI minimization for kidney transplant patients in the maintenance phase to benefit graft function.
Materials and methods: Fifty-six kidney transplant recipients receiving CNI-based immunosuppression (tacrolimus n = 34, ciclosporin n = 22), including those with evidence of pathological CNI toxicity and/or interstitial fibrosis/tubular atrophy, were analyzed. The average post-transplant period at conversion was 7.4 years and all participants underwent transplantation more than 3 years prior, with a mean 22 months of follow-up following EVR administration. Conversion of immunosuppression was accomplished by reducing CNI by 40% and beginning EVR at 1 mg, while the doses of mycophenolate mofetil and steroid remained unchanged. CNI and EVR blood concentrations, as well as graft function were examined, and adverse effects were evaluated.
Results: The concentration of EVR after 1 year was 2.6 ng/ml in tacrolimus patients and 3.3 ng/ml in cyclosporine patients. Significant improvement of graft function was observed quickly after EVR administration, and it had persisted for 1 year after conversion as an 8% increase in eGFR (38.3 to 41.4 mg/dl; $p < 0.005$). Six of 56 patients discontinued EVR due to adverse effects, whereas none of those showed obvious acute rejection.
Conclusion: Late immunosuppression conversion at more than 3 years after transplantation using EVR along with CNI reduction was found to consistently improve graft function in kidney transplant recipients in the maintenance phase.

BO240

CONVERSION FROM TWICE-DAILY TO ONCE DAILY TACROLIMUS IN STABLE KIDNEY GRAFT RECIPIENTS

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Background: Immunosupression has a pivotal role in kidney transplantation (TR). The new prolonged-release formulation (Fm) of tacrolimus (TAC) was developed to provide a more convenient once-daily (OD) dosing to improve patients adherence.
Methods: We selected stable kidney transplant recipients (KTR) that underwent TAC conversion (Cv) in our unit. Clinical and analytical data at and post Cv was analysed retrospectively in order to evaluate the efficacy and safety of Cv from TAC twice-daily (TD) to OD Fm.
Results: We studied 60 KTR, 58.3% male,with mean age 45 $\pm$ 14.5 years,-transplanted between 1996 and 2014. Mean time from TR to Cv was 518 days. Cv was made on a 1 mg:1 mg basis in 66.7% of patients (n = 40) and on a 1 mg:1.1 mg basis in the remaining 33.3%(n = 20).

A statistically significant reduction in TAC blood levels (TBL) requiring an increase in TAC daily dose (TDD) was observed post Cv. Mean change at 3 months was −18.2% for TBL (ng/ml) and +6.4% for TDD (mg/day)($p < 0.05$ versus at Cv in both cases), and at 9 months was −10.2%(ng/ml)and +12.2% (mg/day)($p < 0.05$ versus at Cv in both cases),respectively.

Post Cv TBL reduction >25% was significantly higher in the Cv group 1 mg:1 mg basis (50%;n = 20) than in the Cv group 1 mg:1.1 mg basis (10%; n = 2)($p = 0.004$). However, an increase >25% in post Cv TBL was similar between the two Cv stategies.

No significant change was detected between mean GFR at Cv (57 ml/min) and at 3.6 and 9 months post Cv. Proteinuria and other analytical parameters remained stable with no significant difference at and post Cv. Only one patient (1.7%) had acute rejection due to noncompliance (suspended treatment),and 4 patients (6.7%) discontinued treatment.
Conclusions: OD TAC at similar doses to TD Fm is an efficient and safe treatment option. In spite of associated with TBL reduction that occurred in a short window of values,it was overcome with small increases in TDD. Cv made on 1:1,1 basis seems advantageous.

025 LIVER

BO241 MACROPHAGE INVASION IN HEPATOCELLULAR CARCINOMA ASSOCIATES WITH RECURRENCE AND GRAFT REJECTION AFTER LIVER TRANSPLANTATION

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Background: Tumor-associated macrophages (TAMs) promote tumor progression and have an effect on survival in human cancer. However, little is known regarding their influence on tumor progression, graft rejection and prognosis after orthotopic liver transplantation for hepatocellular carcinoma (HCC).
Methods: We analyzed tumor specimens of HCC ($n = 32$) in hepatectomy specimens for distribution and localization of TAMs, as defined by expression of CD68. Abundance of TAMs was correlated with clinicopathologic characteristics, tumor recurrence and patients' survival after liver transplantation. None of the patients received neoadjuvant radio- and/or chemotherapy prior to transplantation. Statistical analysis was performed using SPSS software.
Results: Patients with high prevalence of TAMs in tumorous tissue (TT) of hepatectomy specimen showed significantly higher graft tumor recurrence following liver transplantation ($\rho < 0.05$). Furthermore, high expression of TAMs in tumor invasive front (TIF) of hepatectomy specimen was associated with increased incidence of graft acute rejection after liver transplantation ($\rho < 0.05$). Tumor recurrence and graft rejection, respectively, were confirmed as independent prognostic variables in the multivariate survival analysis (both $\rho < 0.05$).
Conclusions: Our study provides first evidence that CD68 associates with clinicopathological parameters following liver transplantation for HCC. Tumor recurrence in graft and acute rejection after transplantation were significantly higher in patients with high expressions of CD68 in HCC of hepatectomy specimen. CD68 might serve as a potential biomarker in HCC in the setting of liver transplantation, whereas further studies are needed to elucidate its functional role.

BO243 EFFECTS OF LOCOREGIONAL TREATMENTS BEFORE LIVING DONOR LIVER TRANSPLANTATION ON OUTCOME IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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We evaluated the effects of pre-transplant locoregional treatment on survival in living donor liver transplantation (LDLT), the survival after LDLT in successfully down-staged patients, and the most accurate method for predicting survival after LDLT. From December 2003 to December 2012, 130 patients who were newly diagnosed with hepatocellular carcinoma (HCC) at our hospital underwent LDLT for HCC at our transplant center. Pre-transplant locoregional treatments for HCC were performed in 86 (66.2%) patients. Disease-free survival (DFS) and overall survival (OS) after LDLT, as well as the intention to treat survival after HCC diagnosis in the non-pre-transplant locoregional treatment group, were better than those in the pre-transplant locoregional treatment group. Of the 33 patients with HCC initially beyond the Milan criteria, 12 (36.4%) experienced successful down-staging after locoregional treatments, and the 5-year DFS and OS were 81.8 and 75.0%, respectively, which was comparable to those in patients with HCC initially within the Milan criteria. A bad responder according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) [hazard ratio (HR) = 4.87, 95% confidence interval (CI) = 1.06–22.44, p = 0.04], and increased alpha-fetoprotein (AFP) levels (HR = 4.00, 95% CI = 1.54–10.40, p = 0.004) during pre-transplant locoregional treatments were independent risk factors for HCC recurrence after LDLT in multivariate analysis. In conclusion, liver transplantation may be considered after successful down-staging in patients with HCC initially beyond the Milan criteria, and mRECIST and serum AFP level changes are better selection criteria for LDLT in patients who have received locoregional treatments. Although patients in the non-pre-transplant locoregional treatment group had a better outcome, it may be difficult to conclude and further prospective studies with larger cohorts are required.

BO244 TRANSARTERIAL CHEMOEMBOLIZATION DOES NOT HARM THE HEPATIC ARTERY AT TRANSPLANTATION

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Therapeutic indications for transarterial chemioembolization (TACE) of hepatocellular carcinoma in cirrhotic patients are mainly targeted to reduce tumor burden, bridge patients to liver transplantation (LT) and downstage HCC making patients eligible for LT. TACE may expose hepatic artery (HA) to both mechanical and chemical injuries hence potentially increasing the incidence of vascular complications at LT. The aim of this study is to retrospectively analyze the effect of TACE on HA complications comparing 2 cohorts of patients, TACE group versus no-TACE group, transplanted over the same time period. The 2 groups were homogenous in terms of age, sex, MELD and prevalence of HCV infection and included 73 patients in the TACE group and 198 patients in the no-TACE group. The mean number of pre-LT TACE procedures per patient was 1.5 ± 0.89. The overall prevalence of HA complications was 9.59% in the TACE group and 12.6% in the no-TACE group (p = 0.49). Types of complications occurred were hepatic artery thrombosis (HAT), hepatic artery stenosis (HAS) and hepatic artery pseudoaneurym (HAP) and showed a prevalence of 2.74%, 6.85% and 1.37% vs. 3.03%, 7.07% and 3.53% respectively in the TACE and no-TACE group without any statistical significant difference (p = 0.9 for HAT, p = 0.94 for HAS and p = 0.35 for HAP). Endovascular therapeutic procedures (PTA and stenting) were required in 5.48% of cases in TACE group and in 6.56% in no-TACE group (p = 0.74), while surgery was undertaken in 1.37% in the TACE group and in 3.03% in the no-TACE group (p = 0.44). Moreover the postoperative trend of HA resistive index at colordoppler ultrasound after LT showed no statistically significant difference between TACE and non-TACE groups with values at 1 month of 0.65 ± 0.08 vs. 0.65 ± 0.08 (p = 0.6), 6 months 0.66 ± 0.07 vs. 0.65 ± 0.07 (p = 0.55) and 12 months 0.66 ± 0.07 vs. 0.65 ± 0.07 (p = 0.55). In conclusion, based on our experience, pre-LT TACE is not associated with an increased prevalence of HA complications following LT.

BO245 HCC AND LIVER TRANSPLANTATION – AN INTERDISCIPLINARY CHALLENGE

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Objective: To assess the bridging therapy of patients with hepatocellular carcinoma (HCC) awaiting liver transplantation (OLT) in an interdisciplinary HCC Unit.
Summary Backround Data: The incidence of HCC is increasing worldwide. Almost all HCC patients have a waiting time of more than 6 months until the OLT. For that reason there is a need for a bridging therapy. To optimize the therapy we established an interdisciplinary HCC Unit in 2014.
Methods: All HCC unit patients in 2014 were evaluated.
Results: A total of 250 cases were treated. The 215 men and 35 women had an mean age of 67.7 years. 89% had a cirrhosis with Child-Pugh score (CPS) A in 74%, B in 21% and C in 5%. 33% presented with an unifocal, 17% with a bifocal and 50% with a multifocal tumor. 41% had BCLC Stage A, 40% BCLC Stage B, 16% BCLC Stage C and 3% BCLC Stage D. The causes of cirrhosis were 35% alcohol, 24% NASH, 16% others, 7% cryptogenic, 6% hepatitis B or C, 3% AIH and in 2% haemomochromatosis.

28 of the cases awaiting liver transplantation: 23 men and 5 women, mean age of 56.6 years. All presented with cirrhosis with CPS A in 55.6% and B in 44.4%, no CPS C. 40.7% had an unifocal, 33.3% a bifocal and 25.9% a multifocal HCC. In 62.9% the BCLC stage was A, in 37.1% B, no BCLC stage C or D. The causes of cirrhosis were 32.1% alcohol, 25% NASH, 14.3% hepatitis C, 10.7% AIH and 17.8% others. 4 were treated with OLT, 5 with brachytherapy, 4 with TACE, 3 with SIRT, 2 with RFA. 10 cases received other diagnostics or therapies (LTx evaluation, end endoscopy, MRI, CT, biopsy).
Conclusion: Patients with HCC on OLT waiting list are younger, had a higher CPS and a lower BCLC stage with no difference in the cause of the cirrhosis. They rather presented with unifocal and bifocal tumor nodes.. According to our experience the therapy of patients with HCC requires an interdisciplinary team – especially patients awaiting OLT. Only the interdisciplinary team made an optimal individual treatment possible.

BO246 RADIOLOGICAL RESPONSE AND INFLAMATION SCORES PREDICT TUMOR RECURRENCE IN PATIENT TREATED WITH TRANSARTERIAL CHEMOEMBOLIZATION BEFORE LIVER TRANSPLANTATION

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Background: The characterization of tumor response after transarterial chemoembolization (TACE) in patients awaiting liver transplantation (LT) can identify candidates with favorable tumor biology. Recently, preoperative inflammation scores, such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been related to post-transplant HCC recurrence. We investigated the role of radiological response and inflammation scores in predicting tumor recurrence after LT.
Methods: From 8/2005 to 12/2014, 70 patients treated by conventional (c-TACE, $n = 16$) or Doxorubicin-Eluting Bead TACE (DEB-TACE, $n = 54$) were included. Patients' and tumors' characteristics, including static and dynamic PLR, NLR and alfa-fetoprotein measurements, were reviewed; treatment response was classified according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) or European Association for the Study of the Liver (EASL) criteria as complete (CR), partial (PR), stable (SD) or progressive disease (PD). At pathology, necrosis was defined as a percentage of cumulative tumor area and classified as complete (100%), partial (50–99%) or inadequate (<50%).
Results: According to the imaging before TACE, 22/70 (31.4%) and 12/70 (17.1%) patients were beyond Milan and University of San Francisco (UCSF) criteria, respectively. Complete and partial histological necrosis was achieved in 14/70 (20.0%) and 28/70 (40.0%) patients, respectively. Accuracy between radiological criteria and pathology was 72.9% (51/70) and 68.6% (48/70) for mRECIST and EASL, respectively. Among preoperative variables, mRECIST non-response to TACE at the last imaging before LT [Exp (b)=9.2, C.I. 1.6–51.3, $p = 0.012$], the lack of fulfillment of UCSF criteria before TACE [Exp (b) =4.7, C.I. 1.1–19.3, $p = 0.033$] and an increased (>150) PLR before LT [Exp (b) =5.9, C.I. 1.0–33.9, $p = 0.046$] were independent predictors of tumor recurrence.
Conclusion: mRECIST criteria and preoperative inflammation scores are useful to refine selection of TACE-treated candidates for LT.

BO247 LIVER TRANSPLANTATION IN ELDERLY PATIENTS WITH HEPATOCELLULAR CARCINOMA: IS TIME TO CUT DOWN THE LIMIT?

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Ospedale Niguarda Ca' Granda

Background: Liver Transplantation (LTx) is the best treatment for small Hepatocellular Carcinoma (HCC). Despite the proven benefit of this treatment, only few patients may have access to LTx due to the organs shortage. HCV infection is the first underlying disease in LTx candidates in the west countries. New antiviral drugs have largely demonstrated their efficacy in the definitive cure of HCV. Thus, perspective is an increase of organs availability for other patients not suitable for LTx so far.
Methods: Since January 2000, 400 patients received LTx because of HCC on liver cirrhosis. Among these, 28 patients (7%) where 65 or more years old at time of LTx. In the study period, patients ≥65 were included in the waiting list basing on favorable PS and absence of significant co-morbidity. Twenty-five received a whole liver, instead 3 a partial graft. Mean age was 66 yo (range: 65–68 yo). Twenty patients were male.
Results: After a median follow-up period of 46.8 months, 23 patients are alive and disease free, whereas 5 patients died after a mean period of 16.7 months from LTx. Two patients died because of HCV recurrence, 1 due to graft versus host disease, 1 due to sepsis, 1 due to HCC recurrence. No patients had cardiac or pulmonary complication and their 5 yr survival and disease free survival rates were similar to the entire cohort of <65 yo patients.
Conclusion: Considering the same long term results, limiting the LTx to population of <65 yo people is not more justified. Median life is much longer than 20 years ago and people between 65–70 yo has generally same performance status and clinical condition than people under 65. New drugs for HCV allows to drop patients from waiting list because of HCV cure and allows more livers available for other recipients. In this scenario, expanding the selection criteria for pts with HCC may take in account the possibility to systematically include in LTx program patients quit over 65, particularly for rare blood group (B, AB).

BO248 THE ROLE OF DOWN-STAGING AND BRIDGE THERAPY TO FULFILL MILAN CRITERIA BEFORE LIVING DONOR LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Objective: The role of down-staging/bridge therapy for cirrhotic patients with hepatocellular carcinoma (HCC) exceeding/within Milan criteria before living donor liver transplantation (LDLT) has yet to be defined.
Method: A single-center, retrospective cohort study was conducted on 32 cirrhotic patients with HCC who underwent LDLT from 2000 through 2013. Dynamic three-phase computed tomography (CT) images at initial presentation and just before LDLT were checked whether they met Milan criteria. Final histopathological findings were also reviewed. HCC recurrence and overall survival rates were compared according to tumor status.
Results: Median age, 54 (40–63) years; male: female = 26:6. The most common etiology was hepatitis B/C ($n = 26$). At initial presentation, 9 patients were beyond Milan criteria. Overall, 21 patients underwent pretransplant HCC treatment (bridge therapy, $n = 13$; down-staging, $n = 8$). Transcatheter arterial chemoembolization was the most common modality used ($n = 9$). Of 9 patients beyond Milan criteria, 3 were successfully down-staged, making 6 patients still exceeding Milan criteria at transplant (maximum size, 5 cm; number, 14). Posttransplant histopathological exploration unveiled 13 more patients not meeting Milan criteria microscopically. Overall 5-year survival rate for HCC patients was 72% and equivalent to other indications (78%, $p = 0.25$). Six patients beyond Milan criteria demonstrated significantly worse 5-year recurrence-free and overall survival rates of 50% and 17%, respectively, compared to those within Milan criteria (100% and 75%; $n = 26$). HCC recurrence was observed in 3 patients (all beyond Milan criteria) and they died of disease at 13, 24, and 49 months after transplant.
Conclusions: Successful down-staging therapy provides similar outcomes compared with patients within Milan criteria radiologically, regardless of histopathological findings. The role of bridge therapy warrants further investigation.

BO249 CONFORMAL RADIOTHERAPY AS A BRIDGE TO LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: IS IT SAFE?

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Background: Conformal radiotherapy (CRT) has been proposed as a bridge to liver transplantation (LT) for hepatocellular carcinoma (HCC) unsuitable for standard local therapies, but its effectivness and its impact on perioperative outcome has not been evaluated.
Methods: Perioperative data of 12 patients who underwent CRT before LT for HCC (CRT+ group) were compared to 50 patients who underwent LT for HCC without prior CRT (CRT- group) from March 2012 to August 2014.
Results: Baseline characteristics of the two groups were comparable except for a higher tumor size in the CRT+ group. Mean blood loss was higher in the CRT+ group (1700 vs. 1128 ml, $p = 0.04$). Complete or partial histological response after CRT was observed in 50% and 42% of patients, respectively. One patient in each group died postoperatively. The rate of severe postoperative morbidity was 58% in the CRT+ group and 34% in the CRT- group ($p = 0.19$). Specific anastomosis-related complications (ARCs) occurred more frequently with CRT (42% vs. 14%, $p = 0.04$), comprising 3 associated vascular and biliary ARCs and 2 biliary only ARCs in the CRT+ group; 3 hepatic artery stenosis, 3 biliary leakage and one biliary necrosis associated with portal thrombosis in the CRT- group. Mean hospital stay was 43 ± 27 days in the CRT+ and 32 ± 22 days in the CRT- group ($p = 0.08$).
Conclusions: Conformal radiotherapy before LT is an effective bridging therapy for patients with HCC unsuitable for standard local therapies, with a high rate of histological response. However, the safety of this approach remains questionable, as it is associated with increased surgical difficulties and specific ARCs.

BO250

A POSSIBLE ROLE OF MIRNAS AS PREDICTIVE MARKER FOR THE RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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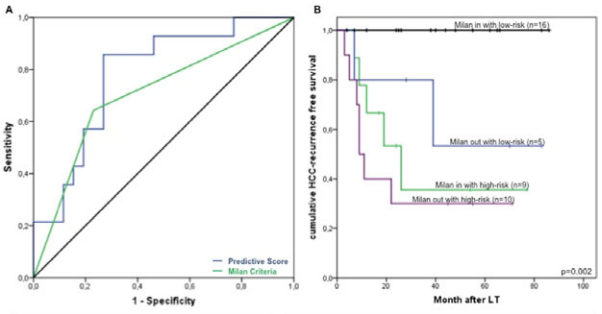
Liver transplantation (LT) is the most radical treatment for hepatocellular carcinoma (HCC) with high rates of long-term survival, yet tumor recurrence after LT remains a challenge. The aim of our study was to identify predictive markers for tumor recurrence after liver transplantation.

In this retrospective single center study all patients who underwent LT for HCC between 01/2007 and 12/2012 were included. Beside demographic data, we analyzed clinical course, bridging therapies, Serum-AFP, time point of tumor recurrence as well as the correlation of imaging and histopathological staging of our recipients. Additionally, we performed a microarray analysis to identify different miRNA profiles of patients with and without HCC recurrence after LT. Single assay stem-loop real-time PCR (Q-RT-PCR) was used for validation of the results.

During the study period 92 LT in patients with HCC (22 women, 70 men) were performed. Twenty-two (23.9%) patients developed recurrence of HCC after LT. This subgroup with tumor recurrence after LT, presented with a mean disease-free survival of 10 months (3–55 months) and an overall survival of 25.5 months (4–77 months). Transplantation outside of Milan criteria, higher AFP levels and higher pathologic grading were associated the tumor recurrence. Performing miRNA analysis, we could identify significant upregulation of 8 miRNAs and downregulation of another 5 miRNAs in patients with tumor recurrence. Consecutively, array data were successfully validated using real-time PCR. Multivariate Cox regression, ROC analysis and Kaplan-Meier showed that a score consisting of two miRNAs and Milan criteria is an independent predictor for tumor recurrence free survival.

Analysis and validation of specific miRNAs combined with radiological parameters might lead to a promising strategy for the prediction of tumor recurrence, but prospective studies have to follow.



	Predictive Score cutoff 20.85	Milan Criteria
Sensitivity	85.7%	64.3%
Specificity	73.1%	76.9%
AUC	0.780	0.709
p value	0.004	0.033

	Milan in low-risk	Milan in high-risk	Milan out low-risk	Milan out high-risk
HCC-recurrence/ No.	0/16	5/9	2/5	7/10
Predictive Score, mean	13.5	28.5	15.2	27.8
Median recurrence free survival (months)	42.0	19.0	39.0	10.0

023 KIDNEY

BO251 SAFE TRANSITION FROM OPEN "ANTERIOR APPROACH" TO HAND-ASSISTED RETROPERITONEOSCOPIC LIVING DONOR NEPHRECTOMY (HARP)

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Introduction: Laparoscopic donor nephrectomy (LDN) is state of the art for living kidney donation. However, non-high volume centers often use the open "anterior approach" (AA). Problems associated to the learning curve of LDN hinder a transition. Aim of this study was to evaluate the learning curve during the process of transition from AA to hand-assisted retroperitoneoscopic donor nephrectomy (HARP) in a non-high volume center.
Methods: Observational study during the introduction of HARP-technique and retrospective comparison to anterior approach donor nephrectomy.
Results: Operation time (OT) and warm ischemia time (WIT) and blood loss (BL) decreased during transition. Pairwise group comparison for OT showed a significant difference for the first 20 out of 50 HARP's only. Graft function was not influenced by the learning process. Comparing 30 consecutive AA's to HARP (procedure 21–50) there was no significant difference in OT (133 ± 24 min vs. 127 ± 19 min, $p = 0.25$) but for WIT (23 ± 28s vs.126 ± 40s, $p < 0.005$) and BL (328 ± 207 ml vs. 54 ± 35 ml, $p < 0.005$). There were neither significant differences in donors' eGFR, CRP and HB-levels nor recipients' eGFR.
Conclusion: In the setting of a non-high volume transplantation center a transition from AA to HARP is possible with a remarkably short learning curve and without additional risk for the donor or loss of quality for the recipient.

Table 1: Pairwise comparison of adjacent groups ($n = 10$ procedures) during the HARP learning period ($n = 50$)

HARP-Quintile (No of procedures, $n = 50$)	Operation time (min) Mean±SD	p value*
1 (1–10)	178 ± 42	x
2 (11–20)	154 ± 23	0.038
3 (21–30)	121 ± 16	0.004
4 (31–40)	140 ± 16	0.09
5 (41–50)	120 ± 17	0.073

BO252 INCISIONAL HERNIA AFTER KIDNEY TRANSPLANTATION: NOT TO UNDERESTIMATE

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Erasmus Medical Center

Background: Incisional hernia is one of the most common postoperative complications after abdominal surgery. Potential risk factors to develop incisional hernia are obesity, abdominal aneurysm of the aorta, use of corticosteroids and postoperative wound infection. Hypothetically, transplant patients may have a higher risk to develop incisional hernia due to immunosuppressive treatment. The objective of this study was to determine the incidence of incisional hernia after kidney transplantation and to identify potential risk factors.
Methods: A retrospective cohort study was performed. All kidney transplant recipients between January 2002 and December 2012 were included. Data were collected using the hospital electronic database. Two groups of patients were identified: patients who developed incisional hernia and patients without incisional hernia. Primary outcome was the incidence of incisional hernia. Risk factor analyses for development of incisional hernia were performed.
Results: A total of 1564 kidney recipients were included. Fifty-one patients (3.3%) developed incisional hernia. On univariate analysis, female gender (53% vs. 35% $p = 0.009$), BMI>30 kg/m^2 (37% vs. 17%, $p < 0.001$), previous abdominal wall hernia (29% vs. 16%, $p = 0.009$), multiple explorations of the ipsilateral iliac fossa (37% vs. 19%, $p = 0.001$) and duration of surgery (209 min vs. 188 min, $p = 0.020$) were associated with the development of incisional hernia. Furthermore, there was no relation between diabetes, immunosuppressive regime, type of donor, prior hemo- or peritoneal dialysis, surgery during afterhours and age of recipients. In multivariate analyses female gender (HR 2.2: $p = 0.007$), past or current smoker (HR 2.1; $p = 0.020$), obesity (BMI >30) (HR 2.9; $p < 0.001$), multiple exploration of the ipsilateral iliac fossa (HR 2.5; $p = 0.002$) and others abdominal wall hernia (HR 2.5: $p = 0.003$) were independent risk factors. Twenty-seven of 51 patients (53%) underwent surgical repair, of which 10 (20%) required emergency repair.
Conclusions: The incidence of incisional hernia after kidney transplantation is 3.3%. Risk factors for the development of incisional hernia are female gender, BMI>30, previous abdominal wall hernias, smoking, multiple explorations and duration of surgery. These risk factors should be taken into account to prevent incisional hernia.

BO253 TRANSPLANTED KIDNEY'S URETERAL VASCULARIZATION ASSESSMENT USING ICG ANGIOGRAPHY

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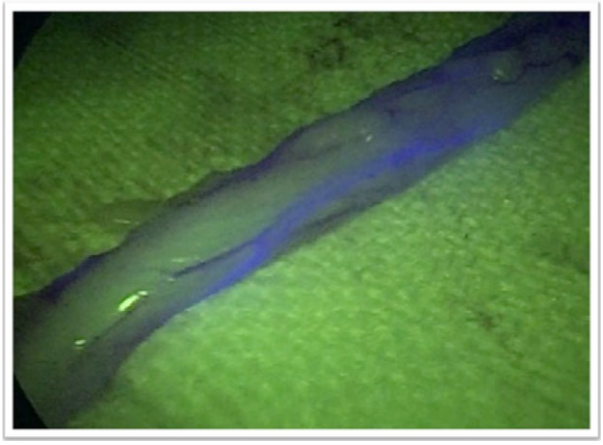
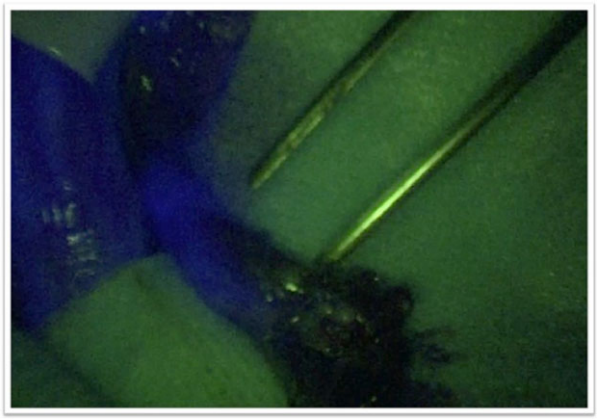
Insubria University Varese OSPEDALE DI CIRCOLO E FONDAZIONE MACCHI

Background: Ureteral necrosis in kidney transplantation remains a rather frequent complication, ranging from 1% to 3% in literature. Ureteral ischemia is the most documented cause of necrosis and should be avoided. Extensive necrosis requires excision of the ureter back to where it is well perfused. Depending on the length of the remain ureter simple reimplantation, a ureteroureterostomy or a ureteropyelostomy can be performed. To help the surgeon ICG (indocyanine green) angiography, can be helpful to detect the ischemic part of the ureter during kidney transplantation and ureter reimplantation.
Methods/Materials: We performed an ureteral ICG angiography during ten kidney tansplantation and during three anastomosis re-do in ureteral necrosis. 5 ml of ICG at a concentration of 0.3 mg/ml/kg was injected intravenously. For ICG fluorescent imaging, we used a laparoscopic system, a 10 mm laparoscope applicable for white light (WL), autofluorescence imaging, and ICG-imaging.
Results: The ten kidney transplantations were successful. ICG angiography demonstrated ureteral blood supply and guide ureteral section before implantation avoiding the risk of distal ureteral necrosis. No post-operative complications, urinary leak and stenosis were detected, creatinine level decrease rapidly.



In all three cases of ureter reimplantation ICG angiography was helpful as well to visualize ureteral vascularization. ICG angiography demonstrated ischemia in the distal part of the ureter around the leak. Re-implantations were successful, no post-operative complications were found, collection and necrosis were avoided.



Conclusions: ICG angiography can be helpful to evaluate the correct vascularization of ureter during kidney transplantation and ureter reimplantation.

BO254

SIMULTANEOUS HAND-ASSISTED TRANSPERITONEAL BILATERAL NATIVE NEPHRECTOMY AND EXTRACAPSULAR TRANSPLANT NEPHRECTOMY IN A PATIENT WITH POLYCYSTIC KIDNEY DISEASE

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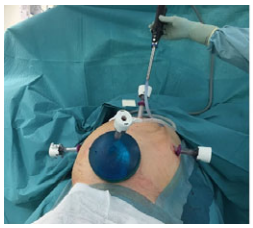
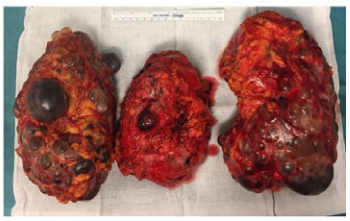
Background: Patients with polycystic kidney disease (PKD) are at increased risk for incisional hernia in particular when voluminous polycystic kidneys are retrieved through large surgical incisions. Here, we preset a hand-assisted transperitoneal minimally invasive technique for simultaneous bilateral nephrectomy and extracapsular transplantectomy in a kidney transplanted PKD patient.
Method: A 48-year-old PKD patient with terminal renal failure underwent kidney transplantation at the age of 28 years. Due to severe graft tuberculosis (Tbc), he lost the graft function after 20 years. Given the large size of the polycystic kidneys and the history of graft-Tbc, we saw the indication for total nephrectomy (native and transplant) in order to maximize the patient's odds for re-transplantation.
Results: With the overall aim to minimize the surgical trauma, we favorized a hand-assisted transperitoneal approach for mobilization and devascularization of both native kidneys and the transplant. The figure illustrates the settings of hand-port and the trocars. A detailed description of the technique will be provided at the congress. Post dissection and devascularizaton, all three kidney were retrieved through the hand-port incision. Importantly, the 5 cm hand-port incision was gradually elongated to retrieve all kidneys without causing contamination issues given the history of graft tuberculosis. The Figure illustrate the size and shape of all three kidneys.
Discussion: To our knowledge, this is the first report of simultaneous bilateral nephrectomy of polycystic kidneys and extracapsular transplant nephrectomy using a hand-assisted transperitoneal technique. By reduction of the surgical trauma and minimization of the incision, this technique might also decrease the risk for incisional hernia in PKD patients.





BO255

FIRST REPORT OF LAPAROSCOPIC KIDNEY TRANSPLANTATION (LKT) IN EUROPE: A SERIES OF 3 CASES

Andrea Sheel[1], Sebastian Gunther[1], Vishwanath Siddagangiah[1], Chang Wong[1], Jean Shallcross[1], Ann Strong[1], Daniel Ridgway[1], Ajay Sharma[1], Abdul Hammad[1], Pranjal Modi[2], Sanjay Mehra[1]
[1]The Royal Liverpool University Hospital; [2]Mehta Institute of Kidney Diseases and Research Centre

Background: Minimal invasive surgery imparts the benefits of less post-operative pain, early recovery and better cosmesis. P Modi (Modi P, et al. Retroperitoneoscopic living-donor nephrectomy and laparoscopic kidney transplantation: experience of initial 72 cases. Transplantation. 2013;95 (1):100–105) has shown the LKT to be feasible and safe. Three Laparoscopic kidney transplants were done following Retroperitoneoscopic donor nephrectomies in September 2014 in Royal Liverpool University Hospital UK.
Methods: Following standard local pre-operative assessment, three suitable patients were selected for live related transplantation.
Results: All 3 kidneys were successfully transplanted laparoscopically on the right side. One patient had previous open appendicectomy and another had previous urological procedures. In both patients, previous incisions were used to insert the kidney intra-peritoneal. In the third patient a 5 cm suprapubic incison was given. We report 23 week follow up data.

Table 1. Summary of patient demographics and 23 week follow up results.

Patient	1	2	3
Gender	Male	Male	Male
Age (years)	51	25	67
Length of stay (days)	6	5	7
Operative time (hours: minutes)	06:05	05:45	05:10
Warm ischaemic time (WIT) (hours:minutes)	01:13	01:24	01:50
Immediate graft function	Yes	Yes	Yes
Age of donor (Age difference) (years)	57 (−6) Female	23 (+2) Female	39 (−28) Female
Kidney used	Left	Left	Right
Total post operative morphine requirements (mg)	24	27	0
Complications	Acute cellular rejection	Antibody mediated rejection	-
Creatinine clearance: 5 days post-operative / 23 weeks post operative	70 / 44	64 / 67	91 / 98

Conclusions: LKT is feasible with satisfactory graft function. Long operative time and WIT was due to logistical reasons which should improve with increasing experience. Interestingly, despite the long WIT, there was primary function in all the kidneys without any surgical complications. Early clinical experience is encouraging.

BO256

URETERAL STENOSIS AFTER RENAL TRANSPLANTATION – A SINGLE CENTER 10-YEAR EXPERIENCE

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Centro Hospitalar do Porto

Background: Kidney transplant (KT) is the definitive treatment for ESRD. Ureteral stenosis (US) is one of the most common urologic complications and has been reported in 2.6–15% of KT.
Methods/Materials: We reviewed data for 973 consecutive KT procedures performed at our center between Jan/2004 and Sept/2014, with evaluation of US management and recurrence rate.
Results: 973 KT performed by direct UV implantation Paquin technique, with a mean follow-up time of 44.3 ± 30.2 [3–111] months. During this period were reported 33 cases of US (3.39%). The interval from KT to US diagnosis was 10.6 ± 23.0 [0.5–98.0] months. Majority of the US were located in the distal ureter and UV junction (83.9%), with only 2 cases of middle ureter stenosis and 2 cases of UP junction. Mean US length of 2.5 ± 1.9 [1.0–10.0] cm.

Surgical management, global and treatment-specific recurrence rates are presented in table 1. Primary surgical treatment recurrence rate was higher for the endoscopic approach, with a mean global time from treatment to US recurrence of 6.9 ± 16.3 [0–65] months and median 2.0 months. Open surgical approach was the main recurrence's treatment option (74%). We report 2 cases of graft loss (6.1%).

US Management		Treatment-Specific Recurrence Rate (RR)	Global RR
Primary Surgical Treatment of US – N = 32			
Baloon dilation	47% (15)	53%	50%
UV Reimplantation	25% (8)	25%	
Single Catheterization	19% (6)	83%	
Ureteroureterostomy (UU) with native ureter	9% (3)	0%	
2nd Surgical Treatment (recurrence) – N = 15			
UV Reimplantation	40% (6)	33.3%	40%
UU with native ureter	28% (4)	25%	
Single Catheterization	20% (3)	66.6%	
Baloon dilation	6% (1)	100%	
Ureteropieloplasty	6% (1)	0%	
3rd Surgical Treatment – N = 5			
UV Reimplantation	40% (2)	0%	0%
UU with native ureter	40% (2)	0%	
Baloon dilation	20% (1)	0%	

Success rate evaluation of overall and treatment-specific primary surgical management did not reveal significant differences ($p > 0.05$) according to stenosis length (3.0 cm), time between transplant and stenosis (≤3; 3–12; >12 months) and stenosis location (distal, middle and upper ureter). However, there was clearly a trend to higher success rate in smaller stenosis (<1.5 cm) and managed early (≤3 months), specifically in baloon dilation.
Conclusion: US management should be decided on a case-by-case basis, according to clinical caractheristics, treatment-specific recurrence rate and previous surgical options.

BO257 BALLOON DILATATION FOR POST-TRANSPLANTATION URETERAL STRICTURES; CASE SERIES

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Erasmus Medical Center

Background: Ureteral strictures are the most common major urological complication after kidney transplantation (KT). In this case series we investigated the effectiveness of balloon dilatation (BD) for ureteral strictures after KT and we tried to determine which patients would benefit from BD.
Methods: This retrospective cohort study was performed in the Erasmus MC, Rotterdam. Data were collected using the hospital electronic database. All surgical and radiological interventions were documented. Based on literature we selected type of ureteroneocystostomy, length and location of the stricture, type of dilatation balloon, stenting after BD and time between transplantation and BD as possible factors that might influence dilatation outcome. Balloon dilatation was considered successful if no other intervention, such as surgical revision of the ureteroneocystostomy or double J placement, was necessary.
Results: We included 28 patients who were treated with BD between august 2007–June 2014 (12 females; 16 males; 6 deceased donors, 22 living donors; mean age at transplantation was 47 ± 15). Median follow up was 49.5 months (3–140). Median time between transplantation and BD was 3 months (1–135). Median length of the strictured segment was 1.25 cm (0.5–5 cm). Fourteen patients (50%) had successful BD (10 patients in 1 attempt and 4 patients in 2 attempts). In 5 patients BD could not be executed successfully due to the impossibility to pass the stricture with the catheter. Univariate analyses did not show any differences in ureteroneocystotomy technique, months between KT and BD, type of balloon used, the length of the stricture, location of the stricture nor the use of a stent (drainage catheter) after BD between the successful and unsuccessful dilatation procedures.
Conclusion: We believe that BD is an effective treatment option for ureterostomy strictures. In our series it is succesful in 50% of the patients and can therefore prevent invasive surgical revision.

BO258 READMISSION WITHIN 30 DAYS POST HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY

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Plymouth NHS Trust

Background: Living donor nephrectomy is a surgical challenge since it involves operating on healthy individuals. Hand assisted laparoscopic donor nephrectomy (HALDN) has replaced the open procedure in many centres and is associated with low morbidity and mortality and quick return to activity.
Methods/ materials: This is a retrospective analysis of prospectively collected data on all HALDN performed at Derriford Hospital between August 2007 and October 2014, focusing mainly on readmission within 30 days of discharge.
Results: A total of 154 (median age: 51 yrs (range: 49–75) donors underwent HALDN during the study period. Fifteen donors (9.7%) were re-admitted to hospital within 30 days following nephrectomy. Overall re-admission rate within 90 days was 11.7%. There was no difference in the median (4 days) and mean hospital stay between the whole and re-admitted group (4.31 vs. 4.76 days). There was also no difference in the median age between both groups. Reasons for readmission include: intra-abdominal collection ($n = 3$), chest infection ($n = 2$), wound infection ($n = 2$), perforated appendicitis and pulmonary embolism ($n = 1$), acute appendicitis ($n = 1$), perforated duodenal ulcer ($n = 1$), acute cholecystitis ($n = 1$), incisional hernia ($n = 1$), vomiting and diarrhoea ($n = 1$), and non-specific abdominal pain ($n = 2$). Four patients required surgery – two for appendicitis, one each for perforated duodenal ulcer and repair of incisional hernia.
Conclusion: The overall readmission rate following HALDN is high compared to published data. The reasons for readmission were unrelated to nephrectomy in 33% with over 15% requiring surgery for complications unrelated to nephrectomy. Living donors should be fully informed about the risks, including the possibility of complications unrelated to HALDN.

BO259 "NIPPLE VALVE" URETEROCYSTONEOSTOMY IN THE TREATMENT OF COMPLICATED VESICOURETERAL REFLUX AFTER KIDNEY TRANSPLANTATION

Dariusz Zadrozny[1], Beata Bzoma[2], Anna Walerzak[1], Justyna Bigda[2], Justyna Kostro[1], Marian Lukianski[1], Alicja Debska-Slizien[2], Zbigniew Sledzinski[1]
[1]Department of General Endocrine and Transplant Surgery, Medical University; [2]Medical University of Gdansk

Despite great improvement in the technique and suturing materials, urological complications are still an important problem after kidney transplantation. Vesicoureteral reflux (VUR) is a common condition in patients after kidney transplantation (KTx) but rarely requires any invasive treatment. Even if VUR causes recurrent urinary tract infection (UTI), adequate therapy with antibiotics, behavior changes and, in some cases prophylactic antibacterial medical care may be successful. However, surgical approach is indicated in some patients suffering from severe UTI.
Aim: The aim of this study is to evaluate the effectiveness of "nipple valve" ureterocystoneostomy (NUC) in the treatment of symptomatic VUR to transplanted kidney. The NUC technique includes ureter implantation on the posterior wall of bladder with „nipple valve" formation from everted ureter over internal stent.
Material and methods: Since 2008 in our transplant outpatients department 25 patients (13M and 12F) treated due to repeated and/or severe UTI accompanied by VUR were identified. In all patients standardized "nipple valve" ureterocystoneostomy with internal stenting was used. The time between KTx and correction varied between 4 and 93 month (mean 39).
Results: No intra- or postoperative complications occurred in this group during NUC operation. Recurrent symptomatic UTI resolved in 25/26 patients after NUC operation. In 1/25 persistent colonization with Klebsiella pneumoniae is still observed, without any need for an antibiotics treatment. Recurrence of VUR (active, grade 3) was proven in 1/25 patient (4%) but without UTI. No case of ureteral stenosis was noted. There were no significant correlations between age, gender, type of immunosuppression and results of treatment with NUC.
Conclusions: "Nipple valve" ureterocystoneostomy is a safe and effective method in the treatment of vesicoureteral reflux complicated with repeated and severe UTI.

BO260 IS THE GRAFT WITH MULTIPLE RENAL ARTERIES INFERIOR TO THAT WITH SINGLE ARTERY FOR THE ASFETY AND THE LONG TERM GRAFT SURVIVAL?

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Backgrounds: Nowadays, it is considered that laparoscopic donor nephrectomy is a gold standard procedure for live kidney transplantation even if the graft has multiple renal arteries (MA). The aim of this study is to compare the surgical complications and short term outcome of renal transplants with single and multiple renal artery grafts, and to clarify the usefulness of laparoscopic procedure for MA cases.
Materials/Methods: From September 2001 to March 2014, 288 retroperitoneal laparoscopic live donor nephrectomies were performed and 18.4% cases had MA. In this study, the cases of intraperitoneal laparoscopic procedure were excluded. We examined demographics, the risk of slow and delayed graft function, the incidence of intra- and post-surgical complications, post-transplant hypertension, acute graft rejection, mean serum creatinine level, and patient and graft survival of both MRA and single renal artery (SA) cases.

Results: Donor and recipient outcomes and complication rates were not significantly different between 2 groups. Only mean cold ischemia time in MA cases was significantly longer than those of SA cases. Especially in MA cases, the pulsatility index (PI) and the resistive index (RI) of each graft area was almost same, and the average of PI and RI was not significantly difference comparing with SA cases.

Conclusion: Kidney transplantation using MA grafts is equally safe as using grafts with SA, regarding graft function, intra- and post-surgical complications, and patient and graft survival. Kidney grafts with MA should not be considered as a relative contraindication and our results warrant the safety and efficacy of the procedure.

013 IMMUNOBIOLOGY/BASIC SCIENCE

BO261 EX-VIVO GENERATION OF ALLOANTIGEN-SPECIFIC REGULATORY T CELLS USING SELECTIVE T-CELL COSTIMULATION BLOCKADE: A COMPARISON STUDY BETWEEN ANTI-CD80/86 MABS AND CTLA4-IG

Masaaki Watanabe[1], Makiko Kumagai-Braesch[1], David Berglund[2], Sara Thunberg[3], Carl Jorns[1], Jarmo Henriksson[1], Torbjörn Lundgren[1], Felix Sellberg[2], Erik Berglund[1], Bo-Göran Ericzon[1]

[1]Division of Transplantation Surgery CLINTEC Karolinska Institutet; [2]Department of Immunology, Genetics and Pathology, Section of Clinical Immunology, Uppsala University; [3]Laboratory Medicine, Karolinska Institutet

Background: Adoptive transfer of alloantigen-specific Tregs generated ex vivo by co-culture with anti-CD80/CD86 mAbs (2D10.4/IT2.2) holds the promise for early immunosuppression withdrawal and graft acceptance after liver transplantation. Belatacept, a clinically approved CTLA4-Ig, may be an alternative agent for the ex vivo generation of donor-antigen specific Tregs. Herein, the effects of anti-CD80/CD86 mAbs (2D10.4/IT2.2) and Belatacept on Treg induction *in vitro* were compared.

Materials and Methods: Human peripheral blood mononuclear cells (PBMCs) were co-cultured with irradiated donor PBMCs in the presence of 2D10.4/IT2.2, or Belatacept in eight different recipient-donor pairs. At day 7, irradiated donor PBMCs, culture media, and 2D10.4/IT2.2, or Belatacept, were replenished. Phenotypes and alloantigen-specific immunomodulatory effects of the generated cells were assessed at day 14.

Results: After 14 days of culture $CD4^+CD25^+CD127^{lo}FOXP3^+$ Tregs increased from 4.1 ± 1.0% to 7.1 ± 2.6% and 7.3 ± 2.6% in the 2D10.4/IT2.2 and Belatacept treated groups, respectively. Generated cells from both treatment groups effectively impeded proliferative responses, in a cell-number dependent fashion, of freshly isolated recipient PBMC against donor-antigen in mixed lymphocyte reactions, while such effect was minor for third-party antigens (Fig. 1). IFN-γ production was downregulated and IL-10 production increased in ELISPOT and ELISA assays from 2D10.4/IT2.2 and Belatacept treated groups, as compared to sham treated cells. Concurrently, delta-2 FOXP3 mRNA expression increased significantly (Fig. 2).

Conclusion: Alloantigen-specific Tregs generated with Belatacept and 2D10.4/IT2.2 show comparable immunomodulatory effects. Belatacept is a promising agent for ex vivo production of clinical grade alloantigen-specific Tregs.

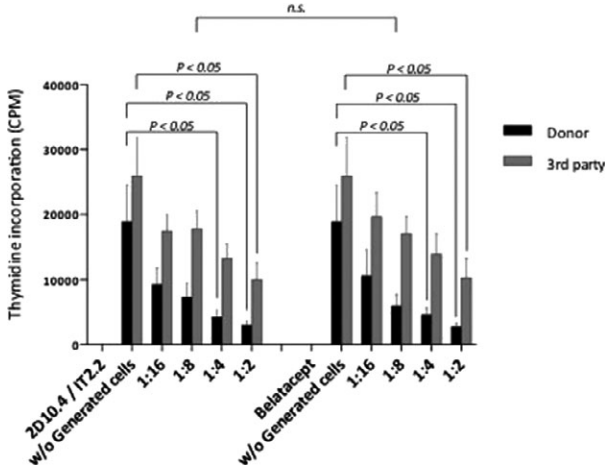

Fig. 1. Proliferation tests. Numbers below x-axes depicts ratio of cultured cell/responder cell.

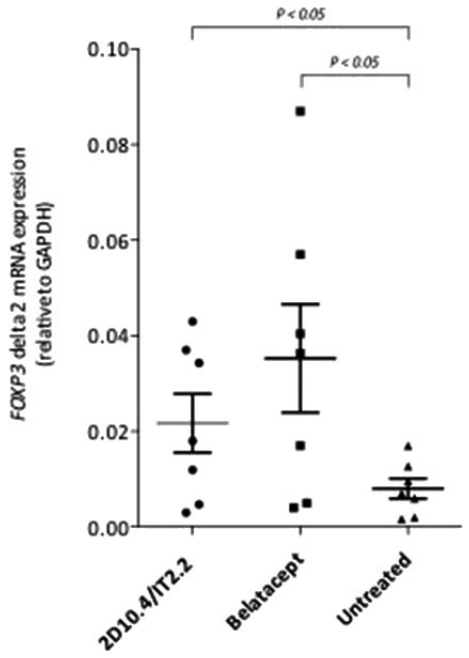

Fig. 2. Induction of delta-2FOXP3 mRNA in co-cultured cells.

BO262 TREG DEPENDENCY OF CTLA4IG MONOTHERAPY IS DOSE-DEPENDENT

Christoph Schwarz, Lukas Unger, Benedikt Mahr, Klaus Aumayr, Nina Pilat, Karin Hock, Andreas Farkas, Ivan Kristo, Thomas Wekerle

Medical University of Vienna

Background: Costimulation blockade with belatacept (CTLA4Ig) has become a valuable treatment option for immunosuppression after transplantation. However, the interaction of belatacept and CTLA4Ig with regulatory T cells (Tregs) has been a matter of debate. Thus, we've investigated the immunosuppressive effect of CTLA4Ig monotherapy in murine heart transplantation (HTX) and explored the role of Tregs herein.

Methods: Murine cervical HTX (Balb/C into B6) was performed with the following dosing regimens of CTLA4Ig, which was injected on days 0, 4, 14, 28, 56, 84, 112: low dose (LD): 0.25 mg (i.e.~10 mg/kg BW); high dose (HD): 1.25 mg; very high dose (VHD): 6.25 mg. Anti-CD25 (PC61, 0.25 mg) was administered on days −6 and −1 (early Treg depletion) or d31 and d36 (late Treg depletion) in selected groups of mice. Grafts were graded according to the ISHLT rejection score. Donor specific antibodies were assessed by flow cytometry.

Results: Chronic CTLA4Ig treatment prolonged allograft survival in a dose-dependent manner (median survival time [MST] untreated: 8 days (d); LD:60d, HD:>100d VHD:>100d; $p = 0.001$). Cessation of CTLA4Ig therapy after 100 days in HD treated mice led to prompt rejection of all grafts (mean survival of 56.3 days from the last CTLA4Ig dose), whereas mice with continuous therapy showed preserved graft function and low histology scores at 200 days ($p = 0.025$) (median ISHLT score 4 vs. 2, $p < 0.001$). Treg depletion with anti-CD25 led to significantly reduced allograft survival when combined with CTLA4Ig LD therapy ($n = 6$, MST: 21.5 days; $p = 0.012$ versus LD without depletion), whereas neither early ($n = 5$) nor late Treg depletion ($n = 6$) under CTLA4Ig HD therapy impacted graft survival (MST>100 days; $p = 0.312$).

Conclusion: A conventional dose-response relationship was observed for the immunosuppressive effect of CTLA4Ig monotherapy in murine heart transplantation. Treg depletion had a negative impact on graft survival only at low, suboptimal doses of CTLA4Ig, but not at higher doses effective in maintaining long-term graft survival.

BO263 *IN VITRO* ACTIVATION IMPROVES THE SUPPRESSIVE CAPACITY OF IL-2 COMPLEX EXPANDED T-REGULATORY CELLS

Karin Hock, Benedikt Mahr, Nina Pilat, Andreas Farkas, Thomas Wekerle

Medical University of Vienna

Background: Tregs applied as cell therapy are under investigation for inducing allograft tolerance. Critical factors like phenotypic and functional differences are linked to the efficacy of Treg therapy. Therefore we investigated

the different Treg populations (natural Tregs versus IL-2 complex expanded Tregs, *in vitro* activated versus fresh) to define the most potent Treg population potentially suitable for clinical use.
Methods/Materials: B6 mice were treated with IL-2 complexes [IL-2/JES6-1]. Tregs were isolated (CD4 + CD25 + Macs Separation Kit) from spleen and lymph nodes from the IL-2 treated and naïve mice ($n = 2$). 1) was cultivated with α-CD3, α-CD28 and IL-2 (*in vitro* activated) and 2) were used without activation (fresh). Cells were analyzed phenotypically by flow cytometry and functionally in a suppression assay.
Results: The yield of the total CD4 + CD25 + isolated cells were around 10 fold higher after IL-2 complex therapy compared to naive mice (IL-2:12 × 106/mouse; naive:1.5 × 106/mouse). Phenotypically the fresh isolated IL-2 Tregs express higher percentage of Helios (80.5 vs. 62), ICOS (71.1 vs. 30.6), Ki67 (43.8 vs. 15.1) and CD44CD62L (37.8 vs. 18.7) in comparison to *in vitro* activated IL-2 Tregs. Whereas both fresh and *in vitro* activated IL-2 Tregs express higher frequencies of ICOS and Ki67 than nTregs. After polyclonal stimulation the *in vitro* activated IL-2 Tregs show significantly better suppressive function compared to *in vitro* activated nTregs (% suppression Treg:Teff 1:2 ratio: IL-2 Tregs79.3 versus nTregs50.1; $p = 0.01$); suppression after allogeneic stimulation was similar. Fresh isolated CD4 + CD25 + cells provide stronger inhibition than fresh IL-2 Tregs but still not as potent as the *in vitro* activated IL-2 Tregs.
Conclusion: The IL-2 complex therapy lead to a high yield of Treg expansion and the *in vitro* activation increases the suppressive capacity of the IL-2 expanded Tregs compared to nTregs. *In vivo* analysis to understand the potency of Tregs is under investigation.

BO264 CD4 + CD28− T-CELLS DECREASE THE RISK FOR EARLY ACUTE RENAL TRANSPLANT REJECTION

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Erasmus University Medical Center

Background: End-stage renal disease (ESRD) patients have a dysfunctional, prematurely aged T-cell system. In this study we hypothesized that the degree of premature T-cell ageing prior to renal transplantation (RT) could predict the risk for early acute allograft rejection (EAR).
Methods: We prospectively analyzed 222 living donor RT-recipients transplanted between 2010 and 2013. EAR was defined as the development of biopsy proven acute allograft rejection within 3 months after RT. As T-cell ageing parameters we determined the T-cell differentiation status, the relative telomere length (RTL) and the number of recent thymic emigrants (RTEs).
Results: Of the 222 patients, 30 (14%) developed an EAR. The median donor age (58 years vs. 52 years, $p = 0.024$) and the historic panel reactive antibody (PRA) score (4% [0–4] vs. 4% [0–29], $p = 0.039$) were higher and the number of related donor RT was lower in the EAR group ($n = 6$ (20%) vs. $n = 82$ (43%), $p = 0.018$). There were no other differences regarding the clinical characteristics, such as the number of HLA-mismatches or the amount of previous RT. Furthermore, no differences regarding the RTL and the number of RTEs were found. The EAR group showed lower number of absolute $CD4^+CD28^-$ T cells (7 cells/μl vs. 21 cells/μl, $p = 0.007$) and a similar trend for the $CD8^+CD28^-$ T cells (83 cells/μl vs. 138 cells/μl, $p = 0.079$). Univariate Cox regression analysis showed that a higher number of $CD4^+CD28^-$ T cells was associated with a lower risk for EAR (HR: 0.65, $p = 0.025$). Multivariate Cox regression analysis (donor age, historic PRA and a related donor RT as covariates) showed that a higher amount of absolute $CD4^+CD28^-$ (HR: 0.66, $p = 0.029$), but not $CD8^+CD28^-$ T cells (HR: 0.99, $p = 0.419$) was associated with a lower risk for EAR.
Conclusion: Premature immunological ageing-related expansion of highly differentiated $CD28^-$ T cells is associated with a lower risk for EAR.

BO265 INTERLEUKIN-34, A NEW ROLE IN REGULATORY T CELL IMMUNOREGULATION AND TRANSPLANT TOLERANCE

Severine Bezie[1], Elodie Picarda[1], Jason Ossart[1], Laurent Tesson[1], Claire Usal[1], Karine Renaudin[2], Ignacio Anegon[1], Carole Guillonneau[1]
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Background: Cytokines, enzymes controlling metabolic pathways and cell surface molecules capable of inducing tolerance have been described. Despite these findings, evidence for other non-identified mechanisms exists and it is thus important to identify new mediators of immune tolerance.
Materiel/methods: PBMC were obtained from blood of healthy volunteers. Lew-1A and Lew-1W rats were used as donor and recipient for transplantation model and *in vitro* cocultures. Recipients were treated with 5.10^{10}pi AdCD40Ig, or 1.10^{12}vg AAVIL-34 and 0.4 mg/day/kg of rapamycin for 10 days, or irradiated 4.5 Gy for adoptive cell transfers.
Results: Flow cytometry analysis revealed that IL-34 is expressed specifically by $CD45RC^{low}CD8^+$ Tregs in rat and $CD45RC^{low}Foxp3^+$ $CD4^+$ and $CD8^+$ Tregs in human. We next demonstrated that IL-34 was involved in rat $CD8^+CD45RC^{low}$ Tregs, by reverting Treg-mediated inhibition of T cell alloproliferation with anti-IL-34 or anti-CD115, but not anti-M-CSF, specific neutralizing antibodies. Furthermore, we proved that both rat and human IL-34 cytokine possess immunoregulatory properties. Indeed, addition of recombinant IL-34 cytokine *in vitro* in a MLR was sufficient to significantly inhibit both human and rat T cell alloproliferation. In addition, overexpression of IL-34 mediated by an AAV vector injected 30 days before transplantation induces cardiac allograft tolerance in 80% of recipients when associated with short term suboptimal dose of rapamycin. Finally, we identified the mechanisms of tolerance induction by IL-34 and demonstrated that IL-34 induced Tregs through modulation of macrophages.
Conclusions: IL-34 is a promising candidate to prevent allograft rejection and induce regulatory cells in transplantation tolerance.

BO267 CHBP REDUCES ACUTE REJECTION BY INHIBITION DENDRITIC CELLS MATURATION THROUGH JAK-2/STAT3/SOCS1 SIGNAL

Cheng Yang[1], Yi Zhang[1], Jina Wang[1], Long Li[1], Lingyan Wang[2], Ming Xu[1], Yaqiu Long[3], Ruiming Rong[1], Tongyu Zhu[1]
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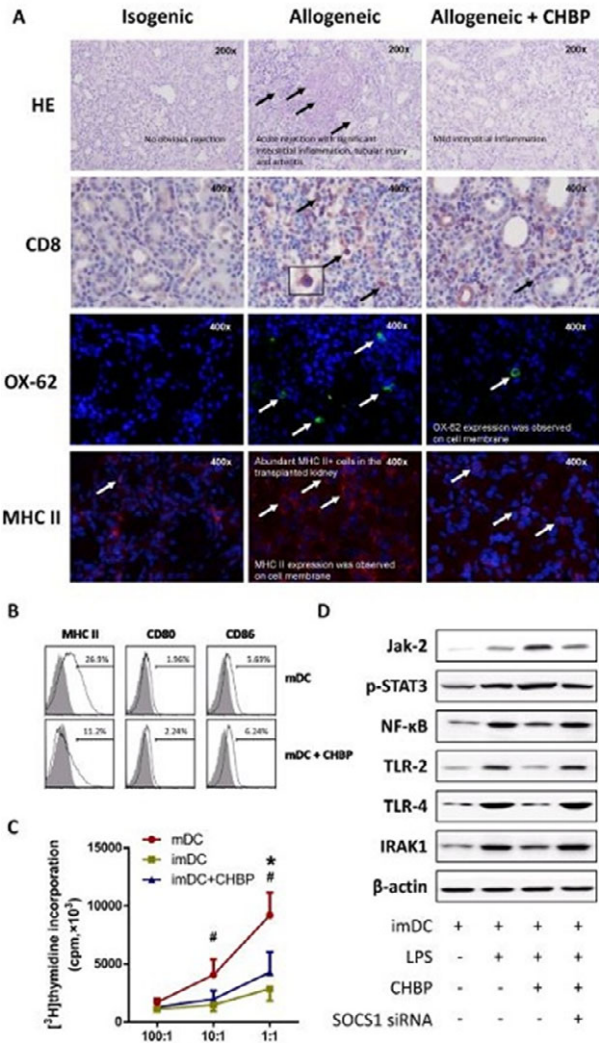
Background: Acute rejection (AR) affects both renal allografts and transplant recipients survival. We recently synthesized a novel proteolysis-resistant cyclic helix B peptide (CHBP), which displays promising renoprotective effects. Dendritic cells (DCs) play an activation role in AR. Thus the present study was designed to investigate the effects of CHBP on DCs in the rat renal transplantation model.
Materials and Methods: The left kidney was harvested from male Lewis rats and transplanted into male Wistar rats with or without CHBP treatment. For *in vitro* experiments, LPS was used to stimulate bone marrow (BM)-derived DCs from Wistar rats with or without CHBP treatment. The phenotype and function of DCs were then evaluated.
Results: Successive five doses CHBP treatment after transplantation significantly ameliorated AR with less histologic injury, CD4 and CD8 T cells infiltration and apoptosis in renal allografts. CHBP reduced IFN-γ and IL-1β protein levels, but increased IL-4 and IL-10 protein levels in serum. The amount of DCs was significantly decreased in renal allografts treated with CHBP, shown as reduced expression of OX-62, MHC-II and CD86. Incubating DCs with CHBP led to reduction of TNF-α, IFN-γ, IL-1β, IL-12 and IL-17, but increasing of IL-10 protein expression in supernatant. Furthermore, CHBP significantly inhibited DC maturation by increasing SOCS1 expression through Jak-2/STAT3 signaling.
Conclusion: CHBP suppresses renal allografts AR by inhibiting maturation of DCs via Jak-2/STAT-3/SOCS1 signaling, suggesting that CHBP could be an effective therapeutic drug for treating AR of renal transplantation.

Figure 1



BO268

IL-7RALPHA BLOCKADE PREVENTS INTESTINAL GRAFT-VERSUS-HOST DISEASE INDUCED BY HUMAN T CELLS IN NSG MICE BY MODULATION OF A4β7 INTEGRIN EXPRESSION

Lyssia Belarif[1], Véronique Daguin[2], Nicolas Poirier[1], Gilles Blancho[2], Bernard Vanhove[1]
[1]EFFIMUNE; [2]UMR 1064

Chronic graft versus host disease (GVHD) remains a major complication of allogeneic hematopoietic stem cells transplantation. IL-7 is a non-redundant cytokine which allows differentiation, survival and homeostatic expansion of T lymphocytes and is implicated in GVHD. Interfering with the IL-7 pathway by targeting the IL7R alpha chain might preferentially impact IL-7Rαhigh effector T cells while sparing regulatory IL-7Rαlow T cells, thereby promoting immune regulation. This was recently demonstrated in pancreatic islets and skin transplantation models in mice.

In this work, we observed that IL-7 is a potent and rapid inducer of integrin α4 and β7 in human but not in mouse T cells *in vitro*. In contrast β1 expression is not affected by IL-7. The lymphocyte α4β7 integrin being the main intestinal lymphocyte homing receptor, we used NOD SCID gamma-/- mice that we engrafted with human PBMC to study intestinal xeno-GVHD. Treatment of recipient mice with antagonist anti-IL-7Rα mAbs for one month (i.p. at 5 mg/Kg biweekly) dampened GVHD and extended survival with a median survival time of 55 days instead of 18 days in control mice ($p < 0.01$), without impacting immune reconstitution. Interestingly, as early as one week post-treatment, the percentage of α4β7 + human T lymphocyte in engrafted human T cells was significantly decreased in comparison with control-treated mice.

These results indicate that IL-7Rα blockade prevents intestinal GVHD in a xenogeneic model. Prevention of the IL-7-induced expression of the α4β7 + integrin is a possible mechanism of action.

BO269

IMPROVED LUNG ALLOGRAFT ACCEPTANCE BY CD26 CO-STIMULATORY BLOCKADE

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Background: CD26 is a co-stimulatory molecule on hematopoietic and somatic cells, responsible for activation and proliferation of T cells. We previously showed that that by inhibiting CD26, lymphocyte infiltration into allografts was markedly reduced and resulted in an amelioration of acute rejection (AR) after mouse lung transplantation (Tx). Here, we analyzed the effects on CD26 co-stimulatory blockade on Th subset cytokines.
Methods: Orthotopic left lung Tx was performed between the MHC class II mismatched mouse strain combination BALB/c (donors) and C57BL/6 (recipients) ($n = 14$). Study groups included control, CD26 inhibited group (CD26-I) with daily administration of a specific CD26 inhibitor, and CD26 KO (CD26KO). Lung transplants and blood samples were assessed on day 1 or 5 post-transplant for blood gas analysis, FACS, and ELISA for Th subset cells and cytokines.
Results: Compared to control, CD26-I and CD26KO showed significantly lower scores in AR grade on day 5 ($p < 0.01$), lower numbers of infiltrating $CD3^+$ T cells in the perivascular and peribronchial area on day 1 and 5 ($p < 0.05$, $p < 0.05$, respectively). In contrast, there were higher numbers of interstitial macrophages in perivascular and peribronchial areas on day 1 ($p < 0.01$). Functionally, CD26-I and CD26KO had higher levels of PaO_2 on day 1 and 5 ($p < 0.05$, $p < 0.05$). ELISA revealed higher levels of IL-10 in allografts of CD26-I and CD26KO than in controls. No differences were found in IFN-γ among groups. FACS analysis showed IL-10^+ cells in grafts to be higher in CD26-I and CD26KO on day 1 ($p > 0.05$) and 5 ($p < 0.05$) post Tx. IL-17^+ cells were relatively less in CD26-I than control on day 1 ($p > 0.05$).
Conclusion: CD26 co-stimulatory blockade in mouse lung Tx ameliorates lung Tx function and results in increased expression of the immunoprotective cytokine IL-10, potentially deriving from alternatively activated macrophages and a reduction of IL-17. This Th balance seems to contribute to lung allograft acceptance.

BO270

LIVE AND DEAD MESENCHYMAL STEM CELLS INDUCE SIMILAR IMMUNOMODULATORY RESPONSES IN HEALTHY AND DISEASED MICE

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There is evolving interest in the use of mesenchymal stem cells (MSC) as a cell therapeutic agent after solid organ transplantation. The nature of the immunomodulatory response after MSC infusion is, however, still largely unknown. The *in vitro* immunomodulatory effects of MSC depend on interactions with immune cells via soluble factors and membrane proteins, which are induced by inflammatory factors. However, recent data demonstrates that MSC have a short survival time after intravenous (IV) infusion, suggesting that the mechanisms of MSC mediated immunomodulation *in vivo* are different. In this study we investigated whether the immunomodulatory effects after MSC infusion depend on the viability of MSC.

To distinguish between effects of live and dead MSC, we heat inactivated (HI) human adipose tissue-derived MSC at 50 °C and examined their immunophenotype and secretome. Immunomodulatory effects of HI and living MSC were evaluated in healthy and LPS-induced septic C57bl/6 mice.

HI of MSC kills MSC without affecting cell surface epitopes and thus keeps the cells intact. Intravenous infusion of live, but also dead MSC in healthy mice induced increased expression of MCP-1, TGF-β and IL-1β in the lungs. Furthermore, systemic increase in MCP-1, G-CSF, IL-5, IL-6 and CXCL1 levels were measured, indicative of an immunomodulatory effect of live as well as dead MSC. In LPS-induced septic mice, infusion of live and dead MSC induced increased IL-10 expression in the lungs. Furthermore, both live and dead cells provoked high serum levels of IL-10 and reduced IFN-γ compared to the PBS controls.

Dead and living MSC induced the same immunomodulatory responses in healthy mice and reduced inflammation in septic mice. These data suggest that, in contrast to *in vitro*, the viability of MSC is not required for the *in vivo* immunomodulatory effect of MSC. Understanding the immunomodulatory mechanisms of MSC treatment will contribute to the development of effective immune therapy.

021 ISLET/CELL TRANSPLANT

BO271 EFFECT OF MIR-7 ON HUMAN PLACENTAL DECIDUA BASALIS TOWARD ISLET LIKE CELL CLUSTERS

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Abstract Functional islet cell replacement is a promising approach for treatment of type 1 diabetes; however, it is limited by a shortage of pancreas donors. Recent studies have demonstrated direct reprogramming of fibroblasts into different types of somatic cell. The pluripotent mesenchymal stromal cells (MSCs) in adult placenta offer an attractive source of stem cells for generation of surrogate beta-cells. Here, we demonstrated that miR-7 and miR-186, a class of small non-coding RNAs, promotes beta cell differentiation of MSCs. Human placental decidua basalis (PDB-MSCs) cells were cultivated from full term human placenta. The imunophenotype of isolated cells was checked for CD90, CD105, CD44, CD133 and CD34 markers. The PDB-MSCs (P3) was separately chemically transfected with miR-7. The qRT-PCR results revealed the expressions of PDX1, KIR6.2, NKX6.1, PAX4, NGN3, GLUT2, insulin, Glucagon and OCT4 genes on the fourth and seventh days after transfection. On the sixth day, the potency of the clusters in response to glucose challenge was tested. Flow cytometry analysis confirmed that more than 90% of cells are CD90 + , CD105 + , CD44 + and negative for CD133 and CD34. Morphological changes were followed from the second day, and cell clusters were formed on sixth day. Islet like clusters showed a deep red color with Dithizone. The expression of pancreatic specific transcription factors were remarkably increased during the four days after transfection and significantly increased on the seventh day. The clusters were positive for NGN3 and insulin proteins and in response to different glucose concentration (2.8 mM and 16.7 mM) the C-peptide and insulin secretion were increased. These results suggest a therapeutic potential for miR-7 as a suitable way for islet cell regeneration.

Keywords: Diabetes, Pancreas, beta-cell, PDB-MSCs, miR-7.

BO272 A NEW 2-STEP PROTOCOL TO ACCELERATE GENERATION OF INSULIN PRODUCING CELLS FROM ADIPOSE-DERIVED STEM CELLS: EFFECT OF HISTONE DEACETYLASE INHIBITOR, VALPROIC ACID

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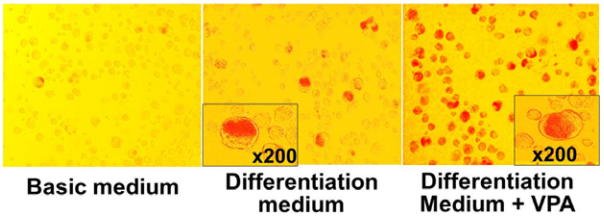
Background: Generation of insulin producing cells (IPCs) remains unsatisfactory because of such as insufficient insulin production by differentiated cells and taking a long time to make differentiated cells. The aim of this study was to establish a new 2-step protocol using histone deacetylase inhibitor (HDAC*i*) to accelerate differentiation of adipose derived stem cells (ADSC) into sustainable IPCs in a short time.
Methods: Rat ADSCs (from DS Pharma Biomedical Co. Ltd, Japan.) were cultured using a modified differentiation cocktail of the previous protocols by addition of 10% of fetal bovine serum, vitamin C during early stage of differentiation, and HDAC*i*, valproic acid (VPA) during late stage. Effect of VPA was investigated by checking the properties of β-cell like cells, such as insulin production and β-cell developmental and endocrine markers. In addition, the concentration of insulin released in to the medium was measured in response to glucose challenge test.
Result: At the end of the differentiation steps (only 28 days), nodular, spindle shaped and fibroblast like cells were observed. Differentiated β-cell like cells were intensely stained by dithizone (DTZ). Number of DTZ positive cells in the differentiation medium plus VPA group was higher (14 + /- 2), in comparison with differentiation medium alone (6 + /- 2) and basic medium (2 + /- 1). Immunofluorescence staining further confirmed the above-mentioned results. The mRNA expression of the β-cell developmental marker NeuroD1 and endocrine markers Insulin1 were more highly expressed in differentiation medium plus VPA group. The differentiated cells with or without VPA secreted insulin differentially and insulin secretion was further increased in the presence of glucose.
Conclusion: Differentiation of ADSC into IPCs could be enhanced by HDACi (VPA), and our new 2-step protocol using VPA-containing differentiation cocktail might be a promising approach to generate IPCs from ADSCs.

Figure: Dithizone staining



BO273 PANCREAS COLLAGEN DIGESTION DURING ISOLATION PROCEDURES FOR ISLET OF LANGERHANS TRANSPLANTATION

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Background: The success of pancreas islet isolation for transplantation depends on various factors such as donor age, body weight, cold ischemia time, and cause of death. The influence of other factors such as the quantity and quality of pancreas collagen is yet unknown. The objective of this study is to develop a tool to quantify pancreas collagen digestion rate and to determine its influence on islet isolation outcomes.
Methods: We analyzed 54 consecutive pancreases and determined the amount of collagen (type I to V) before and after the digestion process. Pancreas digestion was defined as highly effective (<40% of initial collagen amount left after digestion) and poorly effective (≥40% of initial collagen amount). Donor characteristics and isolation outcomes were compared between the two groups.
Results: Donor characteristics were identical in both groups. Initial collagen content was similar in highly effective digestion group vs. poorly effective one (6.5 ± 4.9 mg/g of pancreas vs. 4.8 ± 3.8 mg/g of pancreas, p = 0.194). Post-digestion islet equivalent number (IEQ) was similar in both groups (387'153 ± 210'783 IEQ vs. 364'292 ± 212'675 IEQ, p = 0.709). However, the proportion of post-digestion embedded islets was significantly lower in the highly effective digestion group (22.0 ± 16.0% vs. 35.7 ± 27.0%, p = 0.024). After purification, final yield was significantly higher in the highly effective digestion group (275'524 ± 167'979 IEQ vs. 184'954 ± 85'325, p = 0.037). Recovery rate was non-significantly higher in highly effective digestion group (81% vs. 61%, p = 0.150). Isolation success (i.e. final yield ≥250'000 IEQ) rate was significantly higher in highly effective digestion group (58% vs. 28%, p = 0.046).
Conclusion: A reduction of 40% or more in pancreas collagen initial content following the enzymatic digestion process was associated with successful islet isolation.

BO274 A NON-HAEMATOPOIETIC ERYTHROPOIETIN ANALOGUE PREVENTS DAMAGE TO TRANSPLANTED ISLETS AND INHIBITS MACROPHAGE ACTIVATION

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Background: Pancreatic islet transplantation (PITx) efficiency has been hampered by islet damage during isolation and inflammatory reactions at transplantation. Erythropoietin (Epo) exerts anti-inflammatory, anti-apoptotic and cyto-protective effects in addition to its hematopoietic property. We've investigated if a newly developed non-haematopoietic epo analogue, ARA 290, would protect islets and ameliorate inflammatory responses following PITx.
Methods: Effects of ARA 290 on pancreatic islets of C57BL/6J (H-2b) mice and on murine macrophage were investigated *in vitro* in a culture model. As a marginal PITx, 175 islets were transplanted intraportally to STZ-induced diabetic mice (H-2b). ARA 290 (120 μg/kg) was given intraperitoneally just before and at 0, 6 and 24 h after PITx. Liver samples were obtained at 12 h after PITx, and expression levels of pro-inflammatory cytokines were assessed.
Results: ARA 290 protected islets from cytokine-induced damage and apoptosis. Pro-inflammatory cytokine secretions (IL-6, IL-12 and TNF-α) were significantly inhibited by ARA 290. After the marginal PITx, ARA 290 treatment significantly improved metabolic control. Intra peritoneal glucose tolerance test (IPGTT) performed at day 14, showed significantly lower area under the curve (AUC) in the ARA 290 treated group (Figure1). Up-regulation of MCP-1, MIP-1β, IL-1β and IL-6 mRNA expression within the liver were suppressed by ARA 290 treatment.

Conclusions: ARA 290 protected pancreatic islets from cytokine-induced damage and apoptosis *in vitro* and ameliorated the inflammatory response following PITx. It appears to be a promising candidate for improvement of PITx.

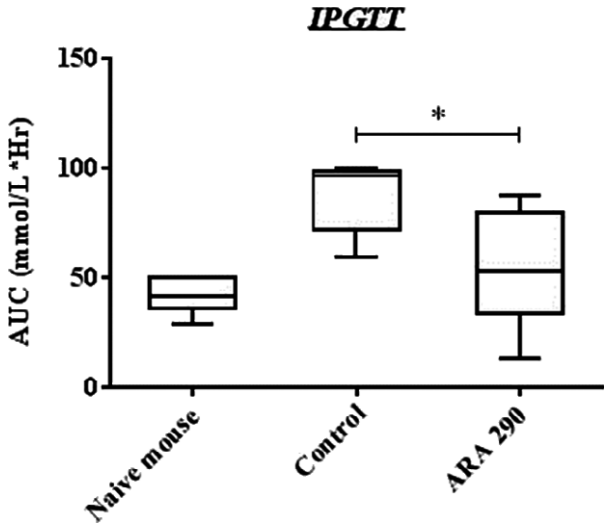

Figure1: AUC in IPGTT is compared among naïve mouse, PITx with PBS (control) and PITX with ARA290 (ARA 290). (*$p < 0.05$ versus control group; values are depicted as lower quartile, median and upper quartile (boxes) with minimum and maximum ranges.).

BO275 VASCULAR SEQUESTRATION OF DONOR-SPECIFIC ANTIBODIES PROTECTS ALLOGENEIC ISLETS FROM HUMORAL REJECTION

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Introduction: Islets grafting restores endogenous insulin production in Brittle type 1 diabetic patients, but long-term outcomes remain disappointing due to destruction of allogeneic islets by recipients' adaptive immune system. In solid organ transplantation, antibody-mediated rejection (AMR) is recognized as the first cause of transplant failure. This experimental murine study aimed at determining whether donor-specific antibodies (DSA) also contribute to islet grafts destruction.
Methods and results: Diabetes was induced by streptozotocine injection in RAG2 KO C57BL/6 (H-2^b) mice, which lack T and B cells. Allogeneic (CBA, H-2^k) islets were not rejected by these immunocompromised recipients, which remained euglycemic until the end of the follow-up (120 days). DSA (either polyclonal immune sera or murine IgG2a anti H-2k mAb) were able to bind to CBA islets and induce complement-dependent destruction β cell line *in vitro*. In contrast, repeated IV injections of DSA did not impact CBA islet grafts function *in vivo*. Live imaging studies, using radiolabelled DSA, showed that alloantibodies were sequestrated in recipients' vascular bed. As a consequence DSA that were able to bind to allogeneic endothelium of CBA heart transplant, failed to reach CBA islets. Indeed, while the vascularisation of transplanted organs comes from the donor, graft vascularisation develops from recipient and is therefore not allogeneic.
Conclusion: Our study demonstrates that, in contrast with solid organ transplants, islet grafts are protected from humoral rejection due to vascular sequestration of DSA.

BO276* ROLE OF BONE MARROW-DERIVED STEM CELLS, RENAL PROGENATOR CELLS AND STEM CELL FACTOR IN CHRONIC RENAL ALLOGRAFT NEPHROPATHY

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Background: Bone marrow-derived stem cells (BMSCs) the hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs) are pluripotent cells that can be mobilized into circulation and recruited to sites of inflammation. The present work was designed to study circulating HSCs,MSCs and renal progenitor cells (RPCs) and stem cell factor (SCF) in patients with chronic allograft nephropathy (CAN) in relation to renal hemodynamics and histopathological changes.
Subjects: This study included 45 subjects, they were divided into three groups each 15, renal transplant patients with stable renal function (Group I), with CAN (Group II) and healthy subjects as controls (Group (III).
Methods: The HSCs and MSCs were identified as CD34 + CD45 + CD117 + and CD34−CD45−CD106+ cells using flow cytometry. Serum SCF levels were measured using enzyme linked immunosorbant assay kit. C-reactive protein (CRP),urinary alkaline phoshatase (U.ALP) were measured. Immunohistochemical staining of renal biopsy was done using monoclonal antibodies against CD133 for detection of CD133 + RPCs, CD34 for detection of CD34 + stem cells,vascular endothelial growth factor (VEGF) as vascular marker and alpha smooth muscle actin (a-SMA) for renal fibrosis. Renal hemodynamics was evaluated by duplex Doppler and resistive and pulsatility indices (RI, PI) were calculated.
Results: There was a significant increase in the level of SCF,number of HSCs,MSCs,RI and PI with a decrease of U. ALP in transplanted patients than the controls. These were positively correlaed with each other and with the markers of renal function. The renal CD133 + and CD34 + cells were positively correlated with each other and with VEGF and negatively with ASMA and fibrosis.
Conclusion: Renal transplantation is assocated with mobilization of BMSCs from the BM into the circulation in parallel with an increased production of SCF with severe kidney injury. The activation of endogenous RPCs may play a role in limiting renal fibrosis and enhancing renal vasculature.

BO277 WHARTON'S JELLY MESENCHYMAL STEM CELLS AMELIORATE CISPLATIN-INDUCED ACUTE KIDNEY INJURY IN MICE

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Background/Aims: Acute kidney injury (AKI) remains a common clinical problem with high mortality rates. Mesenchymal stem cells were so far shown as a promising treatment option. It was recently reported that human Wharton's jelly derived mesenchymal stem cells (WJ-MSC) could ameliorate renal function induced by low dose of cisplatin in rats. However, the role of WJ-MSC in AKI induced with high nephrotoxic dosage cisplatin protocol (comparable to human chemotherapeutic scheme) has not yet been demonstrated. Therefore, we tested whether administration of multipotent WJ-MSC to mice with cisplatin-induced AKI (17 mg/kg body weight intraperitoneally) could improve kidney function and ameliorate damage in the kidney (the outcome through amelioration of apoptosis and induction of tubular proliferative response). The distribution of transplanted stem cells after peripheral infusion was also assessed.
Methods: WJ-MSC were injected intravenously, 24 h after cisplatin application. Cells were labeled with DiI for ex vivo tracing. At 96 h after cisplatin induced AKI, serum creatinine and blood urea nitrogen were measured and renal morphology analysis was assessed by histology to confirm the renoprotective effects of transplanted WJ-MSC. Tubular cell proliferation and apoptosis were identified by immunostaining.
Results: After transplantation of WJ-MSC into mice with cisplatin-induced AKI, improvements in renal function and recovery from tubular epithelial cell injury were observed. Several cells engrafted in renal interstitium in the near vicinity of injured tubular epithelia where they exposed their beneficial effects by decreasing tubular cell apoptosis, with no markable effect on tubular cell proliferation.
Conclusions: Infused WJ-MSC can reach damaged kidney tissue after intravenous transplantation. AKI elicited by lethal dose of cisplatin was considerably improved by WJ-MSC, in parallel with less apoptotic events, with no influence on proliferative response.

BO278 THIRD PARTY MESENCHYMAL STROMAL CELL INFUSION IN KIDNEY TRANSPLANT RECIPIENT: 6-MONTH SAFETY INTERIM ANALYSIS

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Background: Mesenchymal stromal cell (MSC) have immunomodulating properties and could be used as immunosuppressive agents. We report the 6-month safety results for the 5 first patients treated with MSC after kidney transplantation (KTx). Here, we address 3 specific safety issues: immunization against MSC and engraftment syndrome defined as acute graft dysfunction not related to rejection and over-immunosuppression.
Patients and method: MSC production was carried out locally. MSC were not matched with kidney recipients' HLA. Included patients were non-immunized, first transplant recipients from deceased donors. MSC (1.5–3.0 × 106/kg) infusion was planned 3 to 5 days post KTx. Patients with cardiovascular instability post KTx were excluded. All patients were treated with Basiliximab induction, Tacrolimus, Mycophenolate Mofetil and Steroid. We prospectively screened for anti-HLA antibodies at month 1, 3 and 6. Informed consent was obtained from all participants. The local ethical committee approved the protocol.
Results: Collectively there were 23/50 and 29/50 HLA mismatches (MM) with kidney and MSC donor respectively, out of which 5 were shared MM. One patient developed de novo DSA, 2 patients anti-HLA antibodies against shared kidney/MSC MM and 1 patient developed 2 specific antibodies against MSC (MSCSA) at month 6. All antibodies were anti HLA class I except for 1. We did not observe any "engraftment" syndrome. Three patients experienced non-severe opportunistic infections: 1 CMV reactivation and 2 polyoma-BK virus viremia.

Recipient	Age at Tx (years)	63 ± 6
	Gender (M/F)	4/1
	BMI (kg/m^2)	27 ± 3
	Dialysis vintage (days)	373 ± 564
Kidney donor	Age (years)	51 ± 18
	Gender (M/F)	3/2
	BMI (kg/m^2)	26 ± 5
	DBD/DCD	4/1
Transplantation	CIT (min)	737 ± 219
	WIT (min)	46 ± 16
	HLA mismatches (*n*)	
	A (0/1/2)	0/4/1
	B (0/1/2)	1/4/0
	Cw (0/1/2)	1/3/1
	DR (0/1/2)	1/4/0
	DQ (0/1/2)	1/4/0
MSC donor	HLA mismatches (*n*)	
	A (0/1/2)	1/2/2
	B (0/1/2)	1/3/1
	Cw (0/1/2)	0/4/1
	DR (0/1/2)	1/3/1
	DQ (0/1/2)	0/3/2

Conclusion: We did not observe any strong safety signal. We did however observe some degree of immunization in 3 patients: 2 developed antibodies against shared kidney/MSC donor HLA MM and 1 MSCSA.

BO279 MESENCHYMAL STEM CELL TREATMENT IN A MOUSE MODEL OF COMBINED LIVER ISCHEMIA REPERFUSION INJURY AND REGENERATION

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Erasmus Medical Center

Liver ischemia reperfusion injury (IRI) is inevitable during transplantation and extended resections. Hepatic IRI is characterized by hepatocellular injury and hepatocyte loss and may compromise regeneration. At present there is no therapy to treat IRI. Therefore, potential therapeutic strategies to reduce hepatic IRI and accelerate liver regeneration could offer major benefits in both liver transplantation and resection. Mesenchymal stem cells (MSC) are reported to have anti-inflammatory and regeneration promoting properties in models of isolated ischemia or resection. Whether they are of benefit in a more clinically relevant model where IRI is combined with resection induced need for rapid regeneration is currently unknown. Therefore we investigated the effect of MSC administration in a mouse model of combined IRI and partial resection. IRI was induced by occlusion of the blood flow to the left lateral and median liver lobes for 60 min followed by partial hepatectomy of 40% of the liver volume (PH) in C57Bl/6 mice. Animals were treated intravenously with 2-, or 3 x105 mouse syngeneic MSC or PBS control, 2 h before-, or 1 h after IRI. Six hours, and 2- and 5 days after combined ischemia and resection mice were sacrificed. Liver damage was evaluated by measuring liver enzymes, histological damage, and inflammatory markers IL-6 and TNF-α. Liver regeneration was determined by measuring liver/body weight ratio and numbers of proliferating hepatocytes at 2 and 5 days after combined IRI and PH. Liver damage in mice treated with 3 x105 MSC was increased compared to controls. 2 × 105 MSC 2 h before or 1 h after IRI and PH was not significantly different from PBS treated control mice. Liver regeneration was also not different from control animals. In contrast to what is generally assumed, intravenous administration of high numbers of MSC increase liver damage, whereas lower numbers have no beneficial effect on liver IRI or regeneration.

BO280 MULTIPOTENT ADULT PROGENITOR STEM CELL ADMINISTRATION IN A PORCINE MODEL OF EX VIVO LUNG PERFUSION

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Background: Ex vivo lung perfusion (EVLP) is a promising technique to resuscitate potential donor lungs prior to transplantation. Clinical grade multipotent adult progenitor cells (MAPCs) are a novel type of stem cells with immunomodulatory properties. We report our first experience administrating MAPCs during prolonged EVLP comparing intravascular (IV) and intratracheal (IT) administration to modulate ischemia-reperfusion injury.
Materials and Methods: Porcine lungs were perfused for maximum 6 hrs on EVLP following a warm ischemic interval of 90 min. Animals (n = 2/group) were divided in 4 groups. In MAPC-IV group $10*10^6$ MAPCs were administrated IV at onset of EVLP; in CONTR-IV group no cells were added to the perfusate. In MAPC-IT group $10*10^6$ MAPCs in 40 ml PBS were instilled in the airways at onset of EVLP; in CONTR-IT group no cells were added to the PBS. Functional evaluation included the % difference in PVR and Compliance between end and onset of EVLP. Wet-to-dry weight (W/D) ratio was calculated.
Results: Data are depicted as mean.

Not all grafts could be perfused for 6 hrs due to massive edema. Therefore, maximal perfusion time was documented. Decline in graft function was defined as ↑PVR (+%PVR) or ↓compliance (-%COMPL). MAPCs IV further deteriorated lung function and compromised perfusion time compared to CONTR-IV. In contrast, it seems that lung function was better preserved in MAPC-IT compared to CONTR-IT.
Conclusion: These preliminary data indicate that IT administration of MAPCs during EVLP might offer a potential to resuscitate lung grafts. IV administration of MAPCs led to deterioration of pulmonary function in this model. We hypothesize that MAPCs IT might improve epithelial barrier function and modulate the inflammatory response. More data are necessary to confirm these findings and to elucidate potential mechanisms. Results will be updated at time of presentation to n = 6/group.

031 PEDIATRIC TRANSPLANTATION

BO281 OUTCOMES OF ANTIBODY INCOMPATIBLE RENAL TRANSPLANTATION IN CHILDREN – SINGLE CENTRE EXPERIENCE

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Renal transplantation improves quality of life and survival in children requiring renal replacement therapy. A shortage of suitable donors for paediatric patients has driven development of antibody incompatible renal transplantation programmes. The aim of this study was to compare the outcomes of antibody incompatible paediatric cohort with compatible paediatric renal transplants performed in our centre over the same time period.

The antibody incompatible group (AIT) included both ABO ($n = 11$) and HLA incompatible ($n = 2$) renal transplants with the latter defined as having a positive flow-cytometric cross-match prior to desensitization (6 female and 7 male patients). Pre-transplant conditioning was based on our standardized protocol tailored to baseline antibody levels. The control group consisted of 50 randomly selected patients (15 females and 35 male) from our paediatric population transplanted with either living or deceased compatible donor (ACT). The mean age at the time of transplant was 10 years in both groups. We have compared graft survival, biopsy proven rejection episodes, and eGFR.

Death censored graft survival was 100% in the AIT group and 98% in the ACT group (1 graft loss due to antibody mediated rejection). One patient (8%) in AIT group developed acute T-cell mediated rejection successfully treated with anti-thymocyte globulin. One patient who had an ABO and one who had an HLA incompatible transplant experienced an increase in antibody levels. 17 patients (37%) in the ACT group had biopsy proven rejection. There was no statistically significant difference in eGFR measured in ml/min/1.73 m^2 between AIT and ACT patient groups 3, 6 and 12 months post transplant (54.8 vs. 68.3; $p = 0.114$; 54.3 vs. 68.6, $p = 0.224$; 52.6 vs. 65.5; $p = 0.295$).

In our centre the outcomes of antibody incompatible paediatric transplants are not inferior to compatible ones. Good graft survival and acceptable rejection rates make it a feasible option for children awaiting renal transplant.

BO282* RENAL TRANSPLANTATION IN COMPLEX PAEDIATRIC RECIPIENTS WITH VASCULAR ANOMALIES

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Background:
Living donor transplantation is the treatment of choice for children with end-stage renal failure with better long-term graft survival and recipient growth and development than deceased donor renal transplantation. It is therefore usually the preferred option by many units especially as it permits transplantation in more complex recipients. However in children with vascular anomalies transplantation may be difficult especially in small children. We report 5 living donor renal transplants and 1 deceased donor transplant in paediatric recipients with complex vascular abnormalities and significant co-morbidities.
Methods: We retrospectively reviewed 6 complex paediatric renal transplant recipients with respect to technical challenges in view of previous surgery, vascular abnormalities, significant medical co-morbidities and one case of blood group incompatibility. All our living donor kidneys were retrieved by hand-assisted laparoscopic donor nephrectomy technique.
Results: Table 1 summarises the clinical features of the 6 cases. Case 1 and 4 had previous complex vascular reconstructions prior to transplant for mid-aortic syndrome and multiple aortic aneurysms respectively. Case 3 and 4 and 5 also had occluded IVC's, in addition case 4 was a blood group incompatible transplant. All 6 cases were transplanted via a midline approach to the aorta and cava. All grafts functioned well with 2 cases of delayed function (case 4 and 5). There was 1 mortality (case 4 from sepsis 3 months post transplant).
Conclusions: Living donor renal transplantation is feasible and safe in highly complex paediatric recipients with multiple co-morbidities, previous surgery and significant vascular anomalies. A multidisciplinary approach with an experienced anaesthetic, surgical, medical and interventional radiological team is essential for the management of these select cases where more often than not, unconventional surgical approaches may be indicated.

Case	Age at transplant (Years)	Weight (KG)	Co-Morbidities	Pre = Transplant surgical/vascular ISSUES	Implantation procedure	Cold/warm ischaemic times (MINS)	Discharge Cr (μmol/L)
1	9	24	Solitary left kidney. (previous right nephrectomy age 5 yrs), cardiomyopathy	Midaortic syndrome with previous supracoelic aorto-aortic bifurcation Dacron bypass graft & left nephrectomy	Midline approach, graft anastomosed to left common iliac vessels with bladder drainage	208/36	39
2	4	18	De Jeune syndrome ciliopathy, recurrent chest sepsis, chronic liver disease, cardiac dysfunction	Portal hypertension	Midline approach with aorta/cava implant and bladder drainage.	300/30	27
3	7	15	Cong. nephrotic syndrome, bilateral nephrectomies Previous live related transplant (thrombosed).	Recurrent thrombosis with SVC thrombus and occluded infrarenal IVC (collateral drainage), narrow aorta.	Midline, vessels explored intially and aorta/supra renal caval implant performed with bladder drainage. IV heparin infusion.	240/23	46
4	6	18	Multiple aortic aneurysms (repaired) with multiple laparotomies (following trauma), CVA, tracheal stenosis.	2009 repair of aortic aneurysm with extra-anatomincal bypass (PTFE) with jump grafts to Coeliac, SMA and left renal artery.	Midline (adhesions with collaterals present). IVC and common iliacs occluded. Renal vein anastomosed to gondal vein	180/33	graft functioning at discahrge but RIP 3 months post transplant
5	3	14	Trisomy 22, spontaneous GI perforations (one year post transplant) requiring colostomy.	Bilateral renal venous thrombosis with IVC involvement (small calibre IVC with no flow caudal to enterohelpatic portion.	Midline, IVC thrombosed behind liver, no right CIV. Renal vein anastomosed to left EIV, and aortic patch onto distal aorta	1080/30	Delayed graft function with haemodialysis for 10 days post op. Baseline Cr 100.
6	17	34	bilateral ureteronephrosis, thoracotomy for repair	Narrowed entire aorta with internal iliac arterial collaterals.	Midline, supracoeliac deceased donor iliac artery conduit for transplant renal artery	120/30	Immediate function Cr 86 post operative day 4

BO283 COMBINED LIVER-KIDNEY TRANSPLANTATION IN CHILDREN: ANALYSIS OF RENAL GRAFT OUTCOME

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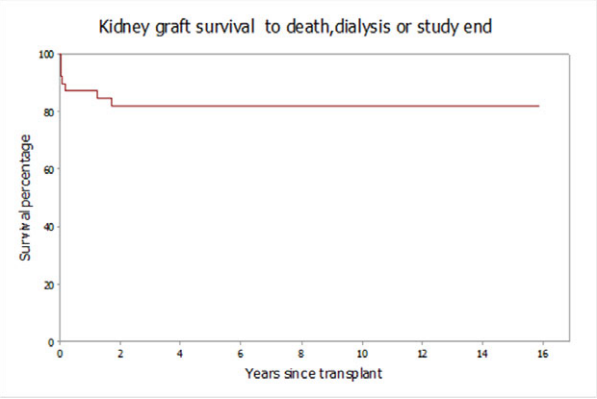
Introduction: Combined liver-kidney transplantation (CLKT) is the accepted treatment for patients with both liver failure and progressive renal insufficiency. Although it remains a relatively uncommon procedure in children, it has become a viable option for rare diseases such as primary hyperoxaluria type 1 and fibro-polycystic liver and kidney disease.

Long term outcome data for CLKT in children is sparse and controversy exists as to whether simultaneous CLKT with organs from the same donor confers immunologic and survival benefit to the kidney allograft. We report the long term renal graft outcome of 40 patients who had simultaneous CLKT.

Method: A retrospective analysis of all paediatric patients (age < 18 years old) who underwent CLKT at our centre from March 1994 to January 2015. Kidney graft survival was defined as time from transplantation to death, return to dialysis or last follow up event. Only histologically proven renal graft rejections were included. Estimated Glomerular Filtration rate (e-GFR) was calculated using the Schwartz formula.

Results: Forty patients had CLKT. The commonest indications for transplantation were fibro-polycystic liver and kidney disease (65%) and Primary hyperoxaluria type 1 (27.5%). Mean age at transplant was 7.3 yrs. (1.3–16.8) and mean weight at transplant was 20.8 kg (9–57). The mean follow up time was 6.1 yrs. (0.02–15.9). Acute renal graft rejection was seen in 2 (5%) patients.

The kidney graft survival was 87.4%, 82% and 82% at 1, 5 and 10 years.



At one year follow up (33 patients), the mean e-GFR was 68.3 mls.min/ 1.73 m^2 (range 28–105.9). The mean e-GFR was 59 mls.min/ 1.73 m^2 (range 31.5–100.5) in 21 patients at 5 years and 50.1 mls.min/ 1.73 m^2 (range 23–86) in 7 patients at 10 years after transplantation.

Conclusions: At 10 years the kidney graft survival was 82% and the mean e-GFR was 50.1 mls.min/ 1.73 m^2 in children with simultaneous combined liver kidney transplants. Histologically proven renal graft rejection was seen in only 5% of children.

BO284* PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION AT KFSH&RC – IMPLEMENTATION OF THE LAPAROSCOPIC RETRIEVAL IN A HIGH VOLUME CENTER

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Since the first successful pediatric liver transplantation was performed in 1967 the survival rate increased from 30% to currently above 90%. This is owed to the introduction of cyclosporine in the early eighties. Another problem was the lack of available size matched liver donors, which caused high death rates on the waiting list of pediatric recipients. Technical innovations based on the segmental anatomy of the liver, e.g. reduced liver grafts, split grafts and living liver transplantation addressed this problem. The last big advantage was the implementation of FK 506 Tacrolimus, which allows steroid withdrawal within the first year post-transplant and preserves the growth potential of children. The new task in living related pediatric liver transplantation is the implementation of the laparoscopic retrieval technique.

Between 2011 and 2014 we performed 156 pediatric liver transplantations with a 92 percentage of living related donors. In our series 38.4% of the children were below one year old with a predominance of genetic-metabolic diseases of 48.2%. In contrast to other countries biliary atresia was the indication for transplant only in 29.5%, 7.1% showed end stage liver disease of unknown reason. Our results show a recipient and graft survival of 93 and 89% respectively. The morbidity was 17% for surgical and 18% for medical complications. The biopsy proven rejection rate was 7%. Six children died after discharge at home or in peripheral hospitals for unknown reasons. In accordance with other centers the rate of grafts from living donors clearly prevails deceased grafts. We implemented the laparoscopic approach in left lateral living donation. The donor complication rate was similar between the minimal invasive and open procedure, while the post donation hospital stay was reduced in the minimal invasive group.

Therefore the laparoscopic retrieval procedure should become standard on the donor side in pediatric living donor liver transplantation.

BO285 BILIARY ATRESIA AND PORTAL VEIN HYPOPLASIA: A HEMODYNAMIC AND HISTOLOGICAL ENTITY

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Background: Biliary atresia (BA) is the most frequent cause of cirrhosis in children, and the main indication of pediatric liver transplantation (LT). Cirrhosis secondary to BA is often associated to a portal vein (PV) hypoplasia (PV caliber ≤ 4 mm), and to severe alterations of liver hemodynamics. We hypothesized that there are histological modifications of native PV in BA, and that these modifications are correlated to native liver hemodynamic parameters.

Methods: A prospective study including 31 cirrhotic children (median age: 0.9 year), transplanted with a living donor was conducted since March 2012; 23 being affected by BA. Native extrahepatic PV was measured invasively during the LT procedure. A study of native liver hemodynamics was done by flowmetry. Gradient between PV pressure and central venous pressure (PVP-CVP) was invasively measured to estimate the severity of portal hypertension. A histological study on native PV was done to quantify the fibrosis of PV wall (measurement of extrahepatic PV wall intima/total wall thickness).

Results: Pre-transplant external PV caliber is significantly smaller in children with BA, with a median PV caliber of 5.5 mm, compared to other cirrhotic children (median PV caliber of 8 mm; p = 0.012). A significant thickening of native PV wall intima was observed in children affected by BA, with a median extrahepatic PV wall intima/total wall thickness of 0.37, compared to a ratio of 0.077 in non-BA cirrhotic children (p = 0.0046). Interesting correlations were observed between native PV wall intima thickening and some pre-transplant liver hemodynamic parameters: pre-transplant external PV caliber (tau = −0.41; p = 0.0019), and pre-transplant PVP-CVP gradient (tau = 0.26; p = 0.038).

Conclusion: PV hypoplasia seems to be a particularity of children affected by BA, with histological modifications of native extrahepatic PV wall. A significant correlation was observed between PV wall histological modifications, and some pre-transplant native liver hemodynamic alterations.

BO286 LIVER HEMODYNAMIC DISTURBANCES IN CIRRHOTIC CHILDREN AS PREDICTIVE FACTORS OF THE NEED TO USE PORTOPLASTY TECHNIQUE FOR PORTAL VEIN RECONSTRUCTION DURING THE LIVER TRANSPLANT PROCEDURE

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Background: Liver hemodynamic disturbances and portal vein (PV) complications are frequently observed in pediatric liver transplantation (LT). A previous retrospective study demonstrated that, in case of PV hypoplasia (PV caliber ≤ 4 mm), PV reconstruction using latero-lateral portoplasty seemed to provide the best technical results. We hypothesized that some pre-transplant liver hemodynamic parameters could predict the need to use portoplasty for PV reconstruction during the LT procedure.

Methods: A prospective study of liver pre-transplant hemodynamics was done in 31 cirrhotic children (median age 0.9 year; range: 0.5–14), 23 being affected by biliary atresia (BA). Hepatic hemodynamic parameters were studied preoperatively by Doppler-ultrasound, and intraoperatively by invasive flowmetry. The technique used for PV reconstruction during the LT procedure was recorded.

Results: Latero-lateral portoplasty was used for PV reconstruction in 17 of the 31 patients included, 15 being affected by BA. Several pre-LT Doppler ultrasound findings were found as good predictors of the need to use portoplasty for PV reconstruction: a median internal PV caliber of 3.2 mm (range: 2.7–4; p = 0.013), a median PV velocity of 7 cm/sec (range: −6.5–16; p = 0.033), and a median pre-transplant arterial resistive index (ARI) of 0.96 (range: 0.9–1; p = 0.025). In the intraoperative period, several findings were also found as good predictors of the need to do a portoplasty for PV reconstruction: a median external PV caliber of 5 mm (range: 4–5.5; p = 0.0047), a median pre-transplant total liver flow/100gr of liver of 23 ml/min (range: 15.5–36; p = 0.003)

	Patients with portoplasty (n = 17)	Patients without portoplasty (n = 14)	p
Internal PV caliber at pre-transplant Doppler (mm)	3.2 (2.7 to 4)	4.8 (3.8 to 7)	0.013
PV velocity at pre-transplant Doppler (cm/sec)	7 (−6.5 to 16)	16.5 (12.5 to 24.5)	0.033
Pre-transplant ARI at Doppler	0.96 (0.9 to 1)	0.84 (0.7–0.9)	0.025
External native PV caliber (intraoperative measure) (mm)	5 (4 to 5.5)	7 (5.5to 9)	0.0047
Total native liver flow/100 g of liver (intraoperative measure) (ml/min)	23 (15.5 to 36)	54 (36 to 75)	0.003

Conclusion: In pediatric LT, latero-lateral portoplasty for PV reconstruction can be used in case of PV hypoplasia, particularly in children with BA. Several non-invasive and invasive native liver hemodynamic parameters seem to constitute potential predictors of the need to do a portoplasty for PV reconstruction during the LT procedure.

BO287 EFFICACY OF INTRAOPERATIVE NEAR-INFRARED RAY NAVIGATION FOR THE EVALUATION OF PORTAL VEIN FLOW IN PEDIATRIC LIVER TRANSPLANTATION

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Background: Portal steal phenomenon lead to the liver graft failure is frequent complication in the case of severe liver cirrhosis in the liver transplantation. Especially, this problems could be more serious because of the large for size graft and severe porto-systemic shunt via collateral vessels in the pediatric liver transplantation. We tried to use infrared ray to evaluate intraoperative portal vein flow and collateral vein flow successfully, and will report our experiences.
Patients and Methods: Total 3 cases with secondary biliary cirrhosisbiliary atresia due to biliary atresia (2 cases) and Alagille syndrome performed living related liver transplantation. Their age is all 1y.o, and donor were 2 fathers and 1 uncle, and average of standard liver volume ratio (%SLV) and graft recipient weight ratio (%GRWR) were 86.6% and 2.7%. all cases with severe porto-systemic shunt were injected indocyanine green (ICG, maximum dose:0.5 mg/body weight) from recipient portal vein and evaluated by Photodynamic Eye (PDE, Hamamatsu Photonics®). Each major collateral vessels which steal portal blood flow were occluded or resected with monitoring PDE images without delay. All cases improved their portal flow and had no complication with postoperative course.
Conclusion: Near-Infrared ray navigation surgery will allows real-time and easy assessment of the portal and collateral flow within vessels during simultaneous surgical manipulation.

BO288 PEDIATRIC LIVER TRANSPLANTATION: AN OUTCOME ANALYSIS OF A 30-YEAR SINGLE CENTER EXPERIENCE

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Introduction: In this study we aim to assess factors influencing long-term patient and graft survival after pediatric liver transplantation.
Patients and Methods: We performed a retrospective analysis of 111 consecutive pediatric liver transplantations (LTx) between 1984 and 2014 at the Innsbruck Medical University. Kaplan-Meier and log-rank analyses were performed to assess 5- and 10-year patient and graft survival.
Results: A total of 55 deceased donor LTx, 15 deceased donor split-LTx, 38 LTx from living donors and 3 multivisceral transplantations performed in children between 3 months and 17 years were included. The median follow-up is 9.13 years. Eleven LTx were retransplantations. Median recipient age was 2.94 years, median donor age was 23 years. Mean anhepatic period was 55.7 ± 20.2 min, the mean cold ischemia time (CIT) was 6 ± 4.06 h. After initial 5-year patient and graft survival rate of 61.4% and 52.1% in the era between 1984 and 1994, the long-term increased to 88.3% and 90.5% graft and patient survival after 5 and 10 years ($p = 0.0008$ and 0.0003) in the era from 2005 to 2014. Five and 10-year patient and graft survival after living-LTx were 97.3% and 94.5%. Graft type, liver disease, donor or recipient age had no significant impact on long-term graft survival. Duration of anhepatic period did not impact patient ($p = 0.439$) and graft survival ($p = 0.354$). CIT above 6 h, however, resulted in a significant lower patient ($p = 0.007$) and graft (0.019) survival. In deceased donor subgroup, recipients younger than 5 years had significant worse 5- and 10-year-outcome (69.6% and 61.9% vs. 88.6% and 83.9% patient survival, $p = 0.020$; 63.2% and 55.3% vs. 85.7% and 81% graft survival, $p = 0.024$).
Conclusion: Excellent long-term results could be achieved. Limited ischemia time, detailed surgical planning and close long-term monitoring are factors influencing the outcome.

BO289 SURGICAL OUTCOMES OF LIVER TRANSPLANTATION IN INFANTS WEIGHING LESS THAN 6 KG

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Introduction: Despite major surgical and medical advances, it is still challenging performing liver transplants (LT) in smaller-size infants. Low-weight is associated with increased risk of vascular complications and reduced patient and graft survival. The aim of this study was to evaluate surgical outcomes of LT for the infants < 6 kg at a single transplant center.
Methods: Of 1009 children < 18 years undergoing LT at our institute from 1989 to Oct 2014, 80 infants < 6 kg were studied. Median age and weight were 4.0 months (range: 6 days–11 months) and 5.0 kg (1.7–5.9), respectively. The indication for LT was biliary atresia ($n = 37$), neonatal hemochromatosis ($n = 20$), cryptogenic hepatitis ($n = 9$), hepatitis B ($n = 3$), and others ($n = 11$). The patients were studied in terms of surgical details, vascular complications and patient survival.
Results: Liver grafts were procured from deceased donor ($n = 68$) and living donor ($n = 12$). Grafts included 37 split, 36 reduced, and 7 whole livers. The overall incidence of hepatic artery thrombosis (HAT) and portal vein thrombosis were 8.8% and 11.3%, respectively. Biliary leak and stricture were 3.8% and 5%, respectively. Six patients underwent retransplantation due to HAT ($n = 4$), chronic rejection ($n = 1$), and cholangiopathy ($n = 1$). The 1, 5, 10-year patient survival was 81.3, 81.3, and 79.4%. Sixteen died after LT due to infection ($n = 5$), multi-organ failure ($n = 4$), primary non function ($n = 2$), pulmonary hemorrhage ($n = 1$), and the others ($n = 4$).
Conclusions: LT in smaller-size infants < 6 kg have acceptable outcomes despite the surgical challenges.

BO290 PLASMA LEVEL OF TRANSFORMING GROWTH FACTOR B1 IN PEDIATRIC LIVER TRANSPLANTATION: CLINICAL AND LABORATORY CORRELATIONS

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Background: Transforming growth factor β1 (TGF-β1) is a pleiotropic cytokine with pro-fibrogenic and immune suppressive properties and may have an impact on liver graft function.
Aim: Analysis of TGF-β1 level in recipients with living donor liver transplantation (LDLT) and its relationship with clinical and laboratory parameters.
Methods/Materials: 130 children (59 boys) aged from 3 to 73 (median 8) months with end stage liver disease (ESLD): 101 patients were transplanted a liver fragment from AB0-compatible (AB0-c) and 29 – from AB0-incompatible (AB0-i) donors. The concentration of TGF-β1, neopterin, sCD30, sCD40L and anti-HLA I/II antibodies were determined via ELISA.
Results: Median level of TGF-β1 in plasma of children with ESLD was 3.4 (min 0.0–max 30.9) ng/ml. LDLT results in increasing of TGF-β1 level in plasma of the recipients to 4.2 (0.4–42.7) ng/ml ($p = 0.02$) and 5.8 (0.2–50.1) ng/ml ($p = 0.001$) one month and one year after LDLT, resp. Plasma level of TGF-β1 before, a month and a year after LDLT did not correlate with gender, age, diagnosis, the disease severity (PELD score) and AB0 compatibility or donor-recipient sex-match, plasma levels of neopterin, sCD30, sCD40L and anti-HLA I/II ab as well as with development of posttransplant complications such as bile fistula, thrombosis and bleeding, rejection episode, viral and bacterial infection. A correlation ($r = -0.23$, $p < 0.05$) between level of TGF-β1 prior to transplantation and the development of graft dysfunction (16 cases) was observed: the cytokine level was lower in recipients with graft dysfunction (2.0 ± 1.3 ng/ml) than in those without dysfunction (5.9 ± 5.1 ng/ml, $p = 0.047$). The relative risk for graft dysfunction with threshold of TGF-β1 value in 3.4 ng/ml was 2.9 ± 0.8 (95% CI 0.6–13.3).
Conclusion: Plasma level of TGF-β1 in the pediatric recipients increases after both AB0-c and AB0-i LDLT. Low blood plasma level of TGF-β1 before LDLT may be a negative predictor of graft dysfunction development.

023 KIDNEY

BO291 DETERIORATION OF RENAL ALLOGRAFT FUNCTION BY EARLY ACUTE GRAFT PYELONEPHRITIS

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Background: Urinary tract infections (UTIs) are the most common bacterial infections in kidney transplant recipients. UTIs complicated by acute graft pyelonephritis (AGPN) are associated with acute kidney injury and renal allograft scarring. However, the influence of AGPN on renal allograft outcome in renal recipients remains controversial.
Material & Methods: Two-hundred sixty-five kidney transplant recipients were evaluated for the impact of early AGPN on renal allograft function between January 2001 and December 2011. Early AGPN was defined as the first AGPN episode occurring within 6 months after kidney transplantation. The changes in estimated glomerular filtration rate (eGFR) over time were compared between patients with and without early AGPN using a linear mixed model. Moreover, Kaplan-Meier (KM) plot and Cox analyses were conducted to evaluate the influence of early AGPN on renal allograft outcome, a reduction in eGFR by 30% over 2 years.
Results: Among the 265 recipients, 30 (11.3%) recipients were diagnosed with early AGPN. During the mean follow-up of 69.1 $\pm$ 28.9 months, 56 (21.1%) patients reached renal allograft outcome, and renal allograft outcome was significantly higher in the early AGPN group (43.3% vs. 18.3%, $p = 0.002$). Moreover, a liner mixed model revealed a significant difference in the rate of eGFR decline over time between the two groups ($p < 0.001$). A Kaplan-Meier analysis showed that renal allograft event-free survival was significantly lower in the early AGPN group ($p = 0.006$). In multivariate Cox regression analyses, early AGPN was found to be an independent predictor of renal allograft outcome (hazard ratio, 2.37; 95% confidence interval [CI], 1.15–4.91; $p = 0.02$).
Conclusions: This retrospective cohort study showed that early AGPN in kidney transplant recipients was independently associated with deteriorating renal allograft function. Thus, this study demonstrates that early AGPN could be a predictor for long-term renal allograft outcome.

BO292 MORNING BLOOD PRESSURE SURGE IN RENAL TRANSPLANT RECIPIENTS: ITS RELATION WITH GRAFT FUNCTION AND ARTERIAL STIFFNESS

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Background: The term that blood pressure rises before awakening in the morning is called as morning blood pressure surge (MBPS). MBPS is considered to be an independent risk factor for cardiovascular diseases. The aim of this study was to investigate the associations between MBPS, graft function, arterial stiffness and echocardiographic indexes in renal transpant recipients.
Materials and Methods: Among 600 renal transplant recipients, 122 patients who had history of hypertension and using at least one antihypertensive treatment. (82 male, mean age: 38.5 $\pm$ 10.7 years) were enrolled into the study. Arterial stiffness was measured by carotid-femoral pulse wave velocity (PWv) by SphygmoCor system and echocardiographic indexes were assessed. 24 h ambulatory blood pressure was monitored for all patients. MBPS was calculated by substracting morning systolic blood pressure from minimal asleep systolic blood pressure.
Results: Mean morning, day time and asleep systolic blood pressure values were 171.2 $\pm$ 23.9, 137.9 $\pm$ 18.1, and 131.7 $\pm$ 18.9 respectively. Dipper hypertention status was in 93 patients. Mean MBPS was 35.6 $\pm$ 19.5 mmHg, mean PWv was 6.5 $\pm$ 2.0 m/sec. Patients with MBPS $\geq$ 35 mmHg (*n*:72, 59%) had significantly lower eGFR (p:0.001) and higher proteinuria (p:0.004) and PWv (p:0.000). Patients with MBPS $\geq$ 35 mmHg had higher left atrium volume (p:0.034) and LVMI (p: 0.002) however systolic and diastolic functions of left ventricule did not show significant difference. In regression analysis; day time systolic blood pressure, asleep systolic blood pressure, morning blood pressure surge, dipper status and left ventricular mass index were detected as the predictors of graft function.
Conclusion: Increased morning blood pressure surge is associated with graft dysfunction, increased arterial stiffness and LVMI that contributes to cardio-vascula

BO293 ARE ANTIAGGREGANT AND ORAL ANTICOAGULANT THERAPIES ASSOCIATED WITH BLEEDING AND VASCULAR COMPLICATIONS IN THE FIRST THREE MONTHS AFTER KIDNEY TRANSPLANT?

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Introduction: Oral anticoagulant (VKA) and antiaggregant (AAT) therapies are common in dialysis patients, but it is not known if they increase the risk of hemorrhagic or thrombotic events in the early post-transplant weeks: we conducted a retrospective analysis on 918 kidney transplant (KTx) to determine whether VKA or AAT are associated with more early (within 90 days) thrombotic (TE) or hemorrhagic events (HE).
Methods: Retrospective analysis on 911 KTRs (51.2 $\pm$ 12.5 years, 572 males = 62.8%) in a single Center. HE included death for bleeding, allograft loss for bleeding, need for surgery to stop bleeding and a number of transfused units > 10 within 90 days after surgery. TE included death for cardiovascular causes, renal arterial or vein thrombosis, renal infarction, myocardial infarction and stroke within 90 days after surgery.
Results: HE were 21/918 (2.3%; 1 death, 4 allograft loss); risk factors for HE at the multivariate analysis were: 1998–2003 year of KTx (OR 5.907, IC95% 1.297–26.903, p 0.0217), HCV positivity (OR 3.300, IC 1.177–9.252, p 0.0232) and VKA (5.548, IC95% 1.768–17.407, p 0.0033); while AAT is not a risk factor. TE were 32/918 (3.5%; 3 death, 11 allograft loss); risk factors for TE at the multivariate analysis were: previous cardiovascular events (OR 4.180, IC95% 1.615–10.948, p 0.0032) and cinacalcet use (OR 7.930, IC95% 3.002–20.945, $p < 0.0001$), while neither VKA nor AAT were a risk factor.
Conclusions: Single or dual AAT are not a risk factor for early hemorrhagic or thrombotic events. VKA is an unmodifiable risk factor for HE, as early parenteral anticoagulation is usually needed (mechanical cardiac valve, thrombophilia). More studies are needed to understand the association between cinacalcet and TE.

BO294 THE CHARACTERISTICS OF POST-OPERATIVE DEEP VEIN THROMBOSIS IN KIDNEY TRANSPLANT RECIPIENTS – DIFFERENCE FROM OTHER TYPE OF SURGERY

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Background: Deep vein thrombosis (DVT) is a severe and common complication that occurs after a major operation. Despite the commonality of DVT, there is limited data on the incidence and characteristics of DVT after kidney transplantation (KT). Further exacerbating the limitations of the existing literature is that most studies have been retrospective in design and were conducted in Western countries. The aim of this study was to evaluate the incidence of lower extremity DVT with mechanical thromboprophylaxis within 1 year of KT in Korean.
Methods: A total of 503 consecutive patients who underwent KT from November, 2009 to October, 2013 were included. The frequency of DVT during the first year after KT was evaluated using serial color duplex ultrasound (CDU) on postoperative days 1 week, 2 week, 4 week, 3 month, 6 month, and 12 month.
Results: DVT occurred in 22patients (4.4%) during this period. All except one DVT were asymptomatic and detected routine scheduled CDU. The timing after transplant is illustrated in Table 1. The incidence of DVT within 1 week is only 18.1% of total DVT and the highest number of DVT (27.3%) occurred in the third months after transplant. On multivariate analysis, recipient age at transplantation (RR 1.059, 95% CI 1.013–1.107, $p = 0.012$) and history of DVT (RR14.468, 95% CI 2.245–93.227, $p = 0.008$) were only significant risk factor for DVT.
Conclusion: Compared with DVT occurred after other type of major surgery, the characteristics of DVT in KT recipients were lower incidence, mild symptoms, and late onset of DVT. These findings suggest that different and longer prophylaxis is required to prevent DVT in KT recipient.

	≤1 week	2 weeks	4 weeks	3 months	6 months	12 months
No of DVT	4 (0.8%)	6 (1.3%)	4 (0.9%)	6 (2.2%)	1 (0.7%)	1 (0.8%)
No at risk	484	475	456	270	151	123

019 ISCHEMIA/REPERFUSION INJURY/PRESERVATION

BO296*

EXTRACELLULAR HISTONES: A NEW BIOMARKER IN KIDNEY TRANSPLANTATION

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Background: Kidneys from donation after circulatory death (DCD) donors are an indispensable attribution to the donor pool, but have a high risk of primary non function (PNF) or delayed graft function (DGF). Clinically useful biomarkers to assess ischemic injury and predict graft viability and transplant outcome are hardly available. Introduced in 2004, cytotoxic extracellular histones are part of neutrophil extracellular traps (NETs) in a mechanism of host defence. Recent *in vitro* studies showed that dying renal cells release histones in the extracellular compartments. Extracellular histones as marker of organ injury and their association to transplant outcome have not been studied. Therefore, we assessed the predictive value of machine perfusate extracellular histones concentration on transplant outcome.
Methods/Materials: We collected machine perfusate samples of 394 machine perfused DCD kidneys. Western blot was used for semi-quantitative analysis of histone concentration (μg/ml). Diagnostic accuracy to predict PNF and DGF was assessed with the area under the receiver operating curves (AURC) and risk of PNF and DGF assessed with regression analysis.
Results: Histone concentrations were not associated with PNF, but associated with DGF in a univariate (odds ratio (OR) [95% confidence interval], 1.791 [1.322–2.425]; $p < .001$) and multivariate (OR 1.526 [1.128–2.064], $p = .006$) regression model. The diagnostic accuracy of histone concentration was poor (AURC = 0.675) in a multivariate model. Histone concentration was not significantly correlated with 1-year graft survival, but did correlate with 1, 2 and 3 years creatinine levels (spearman's rho 0.120, $p = .041$; 0.132, $p = .033$; 0.131, $p = .040$, respectively).
Conclusion: Extracellular histones are a novel biomarker which correlates with transplant outcome, however with poor accuracy to predict DGF after DCD kidney transplantation. Further studies are needed to explore its full potential as new biomarker in transplant medicine.

023 KIDNEY

BO297*

OUTCOME AFTER ECULIZUMAB THERAPY TO PREVENT RECURRENCE OF ATYPICAL HEMOLYTIC UREMIC SYNDROME: EXPERIENCE IN ELEVEN RENAL TRANSPLANT RECIPIENTS

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Atypical hemolytic uremic syndrome (aHUS) is a rare disease with a high recurrence rate after kidney transplantation. aHUS is associated with histological lesions of thrombotic microangiopathy that mainly leads to graft loss. The successful use of Eculizumab (Ecu) to prevent or to treat post-transplantation aHUS recurrence has been scarcely reported. In this study, we describe 11 patients who received a renal transplantation for aHUS and who were treated by Ecu after renal transplantation.

Eleven renal transplants recipients with aHUS on their native kidney received Ecu at our center between 2010 and 2015. Nine patients received prophylactic Ecu at day 0. Two were treated at time of recurrence (day 6 and 25). We reviewed clinical, genetic testing and histological data, and post-transplant course. Mean follow-up was 21.6 $\pm$ 19 months.

Five patients had at least one previous transplantation that failed secondary to recurrent aHUS. A genetic mutation was identified in ten patients (H factor (4); I factor (2), CFH-CFHR1 hybrid gene (1); C3 (1), CFHR1 deletion and anti-H-factor antibody (2)). There was no graft loss and mean serum creatinine was 135 $\pm$ 60 μmol/l at last follow-up. No patient experienced biological thrombotic microangiopathy (TMA) recurrence under treatment. We found transient histological lesions in the 2 patients with later Ecu introduction. Three antibody mediated rejections (AMR) occurred during treatment including one associated withTMA lesions. One patient experienced a C3 glomerulonephritis recurrence.

These data confirm that Ecu is highly effective to prevent post-transplantation aHUS recurrence, without graft loss and with a good renal function. However, Ecu doesn't prevent AMR. The best treatment duration remains to be defined.

BO298

TWENTY-TWO COMPETING DEFINITIONS FOR DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION: A SINGLE-CENTER COMPARISON

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Background: Delayed graft function (DGF) is a severe complication following kidney transplantation. The most used definition, the need for dialysis in the first week post-transplantation, has been challenged by several other definitions. As no gold standard exists, this study compares 22 different definitions and their association with graft failure.
Methods: 497 kidney transplantations from deceased donors at our center between 2005 and 2011 are included. Reasons for exclusion are death of recipient or graft loss within the first week after transplantation. Survival analysis including log-rank tests and Cox proportional hazards model is performed. Sensitivity, specificity, and diagnostic accuracy are calculated to further compare definitions.
Results: Mean follow-up is 5.1 years. All dialysis-based definitions are associated with graft failure and characterized by high specificity (88–97%), but low sensitivity (25–29%). Hazard ratios range from 2.87 to 13.73 with increased risk the more and the earlier dialysis is required. The urine output-based definition performs similar with an association with graft failure and high specificity (96%), but low sensitivity (21%). Serum creatinine-based definitions are more heterogeneous. Higher sensitivity (4–67%) is found in some of these definitions, but is often associated with lower specificity (47–96%), losing the association with graft failure. Definitions combining serum creatinine with either dialysis or urine output vary in sensitivity (17–62%) and specificity (60–96%). However, some of those definitions are able to achieve higher sensitivity without compromising too much on specificity, while keeping the association with graft failure.

Table 1: Competing definitions for DGF

Nr	Definition	DGF	%	Graft failure[1]	Se	Sp	Acc	Log-rank	Hazard Ratio	Cox[1]
Based on dialysis										
1	Need for dialysis in the first week after transplant	no	88%	4% (17/435)	29%	88%	86%	0.008**	3.61 (1.38-9.42)	0.009**
		yes	12%	11% (7/62)						
2	Need for dialysis in the first week after transplant once hyperacute rejection, vascular and urinary tract complications were ruled out	no	88%	4% (18/437)	25%	89%	86%	0.038*	2.87 (1.05-7.86)	0.04*
		yes	12%	10% (6/60)						
3	Need for dialysis after transplant	no	87%	4% (17/431)	29%	88%	85%	0.012*	3.37 (1.29-8.84)	0.013*
		yes	13%	11% (7/66)						
4	Need for dialysis in the first 10 days after transplant	no	87%	4% (17/432)	29%	88%	85%	0.01*	3.45 (1.32-9.01)	0.012*
		yes	13%	11% (7/65)						
5	Absence of life-sustaining renal function that requires dialysis on two or more occasions within the first week after transplant	no	91%	4% (17/453)	29%	92%	89%	<0.001***	6.12 (2.33-16.06)	<0.001***
		yes	9%	16% (7/44)						
6	Need for dialysis in the first 7 days after transplant with specific exclusion of single early post-operative dialysis performed for hyperkalemia	no	88%	4% (17/439)	29%	89%	86%	0.004**	4.03 (1.56-10.4)	0.004**
		yes	12%	12% (7/58)						
7	Return to maintenance hemodialysis within the first 4 days after transplantation	no	96%	4% (18/476)	25%	97%	93%	<0.001***	13.73 (4.76-39.6)	<0.001***
		yes	4%	29 % (6/21)						
Based on SCr										
8	SCr increased or remained unchanged or decreased <10%/day during 3 consecutive days after the transplant	no	46%	3% (8/229)	67%	47%	48%	0.22	1.92 (0.8-4.58)	0.14
		yes	54%	6% (16/268)						
9	CRR2<20%	no	57%	4% (12/282)	50%	57%	57%	0.38	1.22 (0.52-2.88)	0.64
		yes	43%	6% (12/215)						
10	Time required for the kidney to reach CrCl>10 mL/min greater than 1 week	no	91%	4% (18/453)	21%	92%	88%	0.024*	3.85 (1.31-11.3)	0.014*
		yes	9%	11% (5/44)						
11	Failure of SCr to decline in the first 48 h in the absence of rejection	no	89%	4% (18/444)	21%	90%	87%	0.065	2.60 (0.92-7.33)	0.07
		yes	11%	9% (5/53)						
12	SCr >2.5 mg/dL on Day 7	no	75%	4% (14/371)	42%	75%	74%	0.051	2.66 (1.1-6.4)	0.03*
		yes	25%	8% (10/126)						
13	Failure of SCr to fall below pre-transplant levels, within 1 week regardless of the UO	no	96%	5% (23/457)	4%	96%	91%	0.99	1.17 (0.15-9.03)	0.88
		yes	4%	5% (1/22)						
Based on UO										
14	UO <630 ml in the first 24 h	no	95%	4% (18/472)	21%	96%	92%	<0.001***	5.66 (1.97-16.26)	0.001**
		yes	5%	20% (5/25)						
Based on a combination										
15	SCr >2.5 mg/dL on Day 7 or the need for post-transplant hemodialysis	no	73%	4% (14/365)	42%	74%	73%	0.067	2.46 (1.02-5.93)	0.046*
		yes	27%	8% (10/132)						
16	Patients with rise in SCr at 6-8 h post-operatively or <300 cc of urine despite adequate volume and diuretics	no	79%	4% (14/393)	42%	80%	78%	0.005**	2.61 (1.11-6.16)	0.028*
		yes	21%	10% (10/104)						
17	Dialysis requirement after transplant or a SCr 150 μmol/L at Day 8	no	59%	3% (9/293)	62%	60%	60%	0.024*	2.92 (1.2-7.08)	0.018*
		yes	41%	7% (15/205)						
18	UO <1 L in 24 h and <25% fall in SCr from baseline in first 24 h post-transplant	no	92%	4% (20/456)	17%	92%	89%	0.11	2.55 (0.83-7.83)	0.10
		yes	8%	10%(4/41)						
19	UO <75 mL/h in first 48 h or failure of SCr to decrease by 10% in the first 48 h	no	74%	4% (15/370)	38%	75%	73%	0.13	2.04 (0.84-4.96)	0.12
		yes	26%	7% (9/127)						
20	Need for dialysis in the first week after transplant or failure of SCr to decrease within 24 h after transplant	no	81%	4% (15/403)	38%	82%	80%	0.01*	2.64 (1.1-6.31)	0.029*
		yes	19%	10% (9/94)						
21	At least two dialysis sessions or a CRR2 of less than 25% within the first 48 h post-transplant	no	60%	4% (13/298)	46%	60%	60%	0.41	1.18 (0.49-2.86)	0.71
		yes	40%	6% (11/199)						
22	UO <630 ml in the first 24 h and SCr >2.5 mg/dL on Day 7	no	95%	4% (18/474)	21%	96%	93%	<0.001***	6.53 (2.28-18.68)	<0.001***
		yes	5%	22% (5/23)						

Conclusions: Our results indicate a potential advantage of combined definitions for DGF, because they are able to detect a larger group of recipients with an increased risk of graft failure.

BO299

PROSTATE CANCER BEFORE RENAL TRANSPLANTATION: A MULTICENTER STUDY

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Objective: To study the surgical risks of renal transplantation (RT) after treatment of localized prostate cancer (PC) and the oncological outcomes after transplantation in patients on the waiting list with a history of PC.
Method: We conducted a retrospective multicenter study (9 centers) including all patients with PC diagnosed before renal transplantation from December 1993 to July 2011
Results: Forty-three patients were included. Age at diagnosis of PC was 60.6 $\pm$ 6.2 years (45.6 to 72.9). PSA at diagnosis was 8.1 $\pm$ 4.3 ng/ml (4.8 to 20). Thirty-eight patients were treated with prostatectomy: 28 by open surgery, 10 by laparoscopy, with 16 lymph nodes dissection. Five patients were treated by external radiotherapy and two by brachytherapy. Eight patients had adjuvant radiotherapy. Twenty-three, 19, and 1 PC were respectively low, intermediate or high risk according to the classification of D'Amico. The time lapse between PC treatment and RT was 44.4 $\pm$ 29.8 months (14–71). Seven recipients (16%) were transplanted within 24 months after the PC. 29 TR have been described as difficult by the operators (13 external iliac vascular dissections, 16 bladder, and 8 both). Surgical complications post- transplantation were not significantly related to dissections difficulties ($p = 0.2$). No recurrence of PC was observed after a mean follow-up after TR of 36 months
Conclusion: CP discovered before the TR should be treated with RA to assess the risk of recurrence and reduce pending TR. If the CP is at low risk of recurrence, it seems possible to shorten the waiting period before the TR

BO300

MALIGNANCY IN RENAL TRASNPLANT RECIPIENTS – A SINGLE CENTRE EXPERIENCE

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Background: Renal allograft survival rates continue to improve. Consequently, more emphasis is being placed on the long term complications of transplantation. Death from cardiovascular disease in renal transplant recipients appears to be declining although morbidity and mortality from malignancy seems to be increasing. It is well known that the incidence of malignancy is significantly higher in transplant patients although there have been suggestions that incidence is increasing further. This may refect the powerful induction regimes and longer duration of immunosuppression used.
Methods: We conducted a retrospective analysis of all transplant patients who have been followed up within our single centre since 1985. Patients who had died prior to 2000 were excluded due to insufficient data availability. We identified all patients who had been diagnosed with a malignancy following transplantation. We recorded information including transplant type, immuno-

suppression used, donor details, type of malignancy, treatment and outcome. We also considered the duration of immunosuppression, significant virology results, details regarding any rejection episodes and trends in transplant function and immunosuppression levels.
Results: We identified 151 patients who had been diagnosed with a post transplant malignancy. Patients who had a diagnosis of a simple squamous cell or basal cell skin malignancy were excluded from further analysis. This resulted in a cohort of 80 patients. The kidney transplants had occurred between 1973 and 2014. 66% of the cohort were male. The median age of the cohort at the time of their transplantation was 49.5 years and the median age at the time of cancer diagnosis was 60 years. 6 of the patients had 2 or more different malignancy diagnoses. 9 patients (11%) had a diagnosis of post tranaplant lymphoproliferative disorder. Gastrointestinal malignancies of various histological types featured prominently with 16 patients (20%) of the cohort having a diagnosis of either an oesophageal, gastric or colonic malignancy. 12% of patients had a renal malignancy, 7 in native kidneys and 3 in transplanted kidneys. Significantly, 20% of patients had advanced metastatic disease. 55 of the patients are deceased with malignancy being implicated in the cause of death for most.
Conclusion: It is difficult to compare malignancy rates in our small single centre study to rates of malignancy in the general population. However, there are some useful and interesting findings. The incidence of gastrointestinal and renal malignancies is high. However, the malignancies were of varying histological type making conclusions difficult to draw. There did not appear to be a clear correlation between the immunosuppression regime used and the subsequent type of malignancy. This study helps to highlight the importance of close monitoring and surveillancewhen managing the transplant population and questions whether specifically developed screening tools would be appropriate.

BO301 NATIVE KIDNEY FUNCTION AFTER RENAL TRANSPLANTATION IN PRE-EMPTIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: Pre-emptive kidney transplantation (PEKT) for patients with chronic renal failure has several advantages over kidney transplantation for patients with end-stage renal disease (ESRD) on dialysis, and PEKT is a tendency of the worldwide increase. However, the transition of native kidney function after renal transplantation in pre-emptive transplant recipients is not sufficiently investigated.
Methods: We prospectively studied the native kidney function in 10 pre-emptive renal transplant recipients using dynamic MAG3 radioisotope scanning. Renal scintigraphy was performed at pre-transplantation (control), 4 months, and 1 year post-transplantation in all the cases to evaluate the functional contribution of native kidneys after transplantation.
Results: The uptake of radioisotope by the native kidneys was significantly reduced after transplantation, and effective renal plasma flow (ERPF) was lost at 4 months after transplantation in nine patients. In one patient with stage 4 chronic kidney disease (CKD) at the time of transplantation, both the uptake of radioisotope and the ERPF remained at about 80% at 1 year after transplantation, compared with that of a control subject.
Conclusion: The transition of residual native kidney function in pre-emptive renal transplant recipients varies depending on the pre-transplant renal function and the medical background of the patients. Further research should be performed to identify the optimal timing for pre-emptive kidney transplantation in ESRD patients.

BO302 RISK PREDICTION MODELS FOR DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION: ACCURACY IN A SINGLE-CENTER COHORT WITH LOW INCIDENCE

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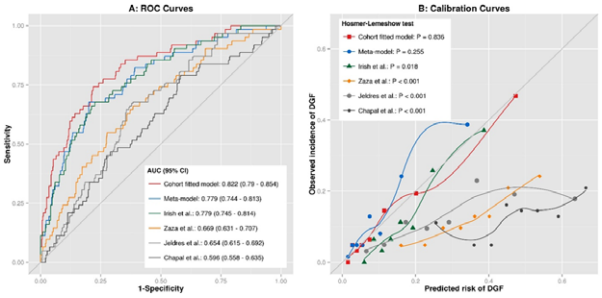
Background: As delayed graft function (DGF) after kidney transplantation is associated with deleterious short-term and long-term consequences, we want to assess the accuracy of four existing predictive models (M1: Irish et al.; M2: Jeldres et al.; M3: Chapal et al.; M4: Zaza et al.) and identify contributing risk factors for DGF.
Methods: 497 kidney transplantations from deceased donors at our center between 2005–2011 are included. The existing models are aggregated into a meta-model (MM) using stacked regressions. The association between 47 risk factors and DGF is studied in our cohort fitted model (CFM) using logistic regression. The predictive accuracy is assessed by area under the receiver operating characteristic curve (AUROC) and Hosmer-Lemeshow test.
Results: The observed incidence of DGF is 12.5%. The CFM indicates that donation after cardiac death (OR 8.67; $p < 0.001$), recipient ejection fraction <40% (OR 3.88; $p < 0.001$), increased donor terminal serum creatinine (OR 3.05 per 1 mg/dL; $p < 0.001$), higher donor age (OR 1.37 per 10 years; $p = 0.006$), longer duration of dialysis (OR 1.24 per 1 year; $p = 0.02$) and higher recipient BMI (OR 1.09 per 1 kg/m^2; $p = 0.008$) are significantly associated with DGF. Higher donor BMI (OR 0.91 per 1 kg/m^2; $p = 0.041$) and higher recipient preoperative diastolic blood pressure (OR 0.78 per 10 mmHg; $p = 0.049$) are inversely associated with DGF. M1, M2, M3, M4, MM and CFM have AUROCs of 0.78, 0.65, 0.59, 0.67, 0.78 and 0.82 respectively. M1 ($p = 0.018$), M2 ($p < 0.001$), M3 ($p < 0.001$) and M4 ($p < 0.001$) overestimate the risk. MM ($p = 0.255$) and CFM ($p = 0.836$) are well calibrated.



Conclusion: Four existing predictive models for DGF overestimate the risk in a cohort with a low incidence of DGF. Logistic regression results in a model of eight significant parameters having a strong discrimination and calibration. Two of these parameters are not included in previous models: recipient ejection fraction and recipient preoperative diastolic blood pressure.

BO303 KIDNEY TRANSPLANT IN LUPUS NEPHRITIS: OUTCOMES IN A COLOMBIAN COHORT

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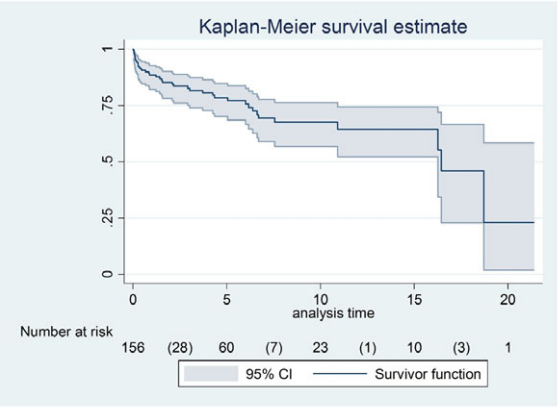
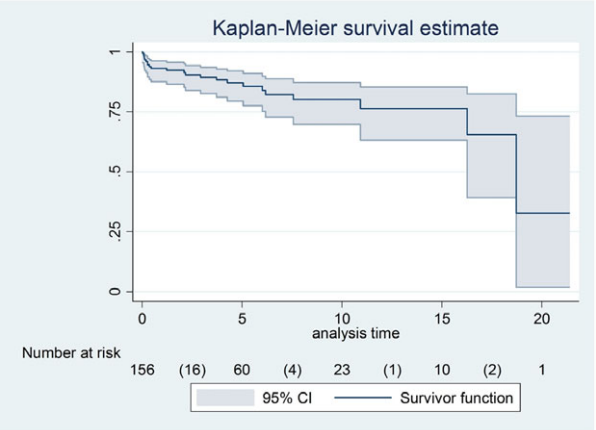
Background: Few data are available about the long-term outcome of kidney transplantation in Hispanic patients with systemic lupus erythematosus (SLE).
Objective: To determine the epidemiological profile and outcome of patients with lupus nephritis (LN) undergoing renal transplantation.
Methods: We retrospectively studied all SLE patients who received kidney allografts in our center between august 1977 and December 2013. Patient and allograft outcomes were assessed as well as rate of clinical recurrence lupus nephritis (RLN).
Results: We included 185 patients in the study, the overall patient survival rates were 88% at 1 year, 82% at 3 years, 78% at 5 years and 67% at 10 years. Graft censored survival rates were 93% at 1 year, 89% at 3 years, 87% at 5 years and 80% at 10 years. Recurrence of lupus nephritis was documented in 2 kidney allograft (1.08%). Multivariate regression analysis showed the following factors to be independently associated with lower patient survival: age had a HR 1.05 (CI 95%: 1.01–1.09, p 0.008) and 1-month serum creatinine a HR 2.22 (CI 95%, 1.51–3.28, p 0.000). We also founded that use of induction therapy provides a better survival for patients, HR 0.35 (CI 0.13–0.94, p 0.038). For graft survival: age HR 1.07 (CI 95%, 1.02–1.12, p 0.006) and 1-month serum creatinine a HR 2.29 (CI 95%, 1.39–3.76, p 0.001). We found a trend of better patient and graft survival in those who received micophenolic acid instead of azathioprine with a p value of 0.05.
Conclusion: Long-term patient and graft survivals in our cohort of Hispanic patients are comparable with those reports in Caucasian. Clinical RLN is very low and our data demonstrate that kidney transplant is a safe alternative therapy for ESRD in this population.

Age	32.8 ± 10 years
Female	158 (85.4%)
Time since SLE	110.5 ± 87 months
Previous Renal Replacement Therapy	112 (60%)
Time on Dialysis	32.2 ± 56.4 months
Follow Up	4 years IQR (1–8)
Time on wait list	5 months IQR (2–12)
Deceased Donors	152 (82%)
Cold Ischemia	21.2 ± 10 h
HLA mismatch	4.0 ± 1.1
Induction Agents	81 (44%): Alentuzumab 43 (53%)
Triple inmunosupressant therapy	158 (86%) Most common (Csa + AZA or MMF + steroids in 142: 77%)
Acute rejection	49 (26.4%) Mild Rejection Bor-IA-IB 40 patients
Recurrence of Lupus Nephrits	2 (1.08%) Bothcases were Membranous Lupus Nephritis (Type V)
Mortality	39 (21%) including 24 deaths with functional graft (61%)
1 year patient survival	88%
5 year patient survival	78%
10 year patient survival	67%
1 year censored graft survival	93%
5 year censored graft survival	87%
10 year censored graft survival	80%
COX RM for Mortality: Age	HR 1.05 (CI 95%: 1.01–1.09, p 0.008)
COX RM for Mortality: Serum Creatinine 1st Month	HR 2.22 (CI 95%, 1.51–3.28, p 0.000)
COX RM for Mortality: induction therapy	HR 0.35 (CI 0.13–0.94, p 0.038)





BO304

PREEMPTIVE KIDNEY TRANSPLANTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER EXPERIENCE

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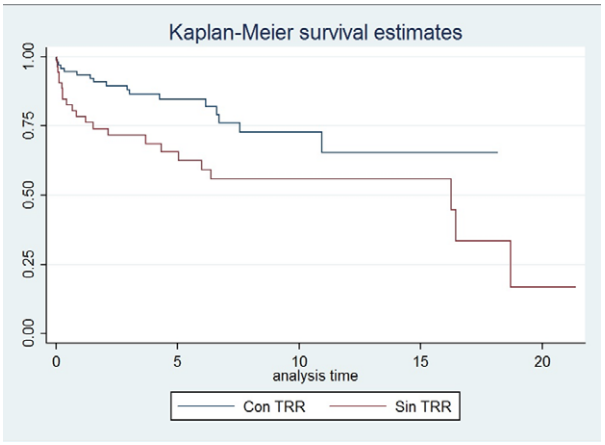
Background: Most kidney transplant (KTX) recipients undergo maintenance dialysis before transplantation. Preemptive KTx (PET), defined as transplantation performed before initiation of long-term dialysis, is controversial. Patients with kidney failure due to systemic lupus erythematosus (SLE) may not receive a PET because of concern for disease activity and shortened graft and patient survival.
Objetive: To compare kidney transplant and recipient outcomes in preemptive and nonpreemptive recipients with kidney failure due to SLE.
Methods: We retrospectively studied all SLE patients who received KT in our center between august 1977 and December 2013. Main outcomes were assessed.
Results: We included 180 patients in this analysis, 68 patients witn PET and 112 nonpreemptive recipients. We excluded 5 patients who a PET was intended but undergo dialysis for a period inferior to 3 months. The overall PET survival rates were 78% at 1 year, 72% at 3 years, 66% at 5 years and 56% at 10 years compared to nonpreemptive recipient survival rates were 85% at 1 year, 76% at 3 years, 72% at 5 years and 61% at 10 years which was signficantly worse for preemptive SLE KT p 0.015 (see figure 1). PET graft censored survival rates were 88% at 1 year, 83% at 3 years, 79% at 5 years and 71% at 10 years. Multivariate regression analysis showed that the only factor associated with lower patient survival was 1-month serum creatinine a HR 2.51 (CI 95%, 1.49–4.23, p 0.001). For graft survival: age HR 1.08 (CI 95%, 1.0–1.18, p 0.053) and 1-month serum creatinine a HR 2.34 (CI 95%, 1.25–4.38, p 0.008). The main difference in mortality was seen during the first year of transplant: 11 deaths in the pET versus 6 in the nonpET group. The main cause of death in the PET was infection.
Conclusion: Preemptive KT in SLE patients may have an increased risk of death during the first year of transplant, especially from infection.



Variable	Preemptive SLE patients $n = 68$	Non Preemptive SLE patients $n = 112$	p value
age	32.1 ± 10.2 years	33.2 ± 10.6 years	0.519
Female	56 (82%)	99 (88%)	0.256
Time since SLE (months)	84 (38–144)	84 (48–144)	0.556
On wait list (days)	168 (59–360)	154 (60–351)	0.460
Deceased Donor	52 (79%)	96 (86%)	0.233
Donor creatinine (mg/dl)	0.97 ± 0.32	0.99 ± 0.70	0.850
Cold ischemia time (h)	21 (16–26)	19 (16–25)	0.191
Induction Therapy	24 (36%)	56 (50%)	0.065
CsA + MMF Or AZA + PDN	48 (72%)	89 (80%)	0.207
1 month serum creatinine	1.8 ± 1.1 mg/dl	1.5 ± 0.7	0.048
Acute Rejection	15 (22.05%)	33 (29.4%)	0.359
Mortality	22 (35%)	17 (18%)	0.017
Death from infection during first year	6/11 (54.5%) 6/22 (27.2%)	3/6 (50%) 3/17 (17.6%)	0.745
Patient Survival at 1 year	78%	85%	0.03
Patient Survival at 3 year	72%	76%	0.04
Patient Survival at 5 year	66%	72%	0.03
Patient Survival at 10 year	56%	61%	0.10
Graft Censored Survival at 1 year	88%	93%	0.04
Graft Censored Survival at 3 year	83%	89%	0.04
Graft Censored survival at 5 years	79%	89%	0.01
Graft Censored survival at 10 years	71%	80%	0.01

BO305

KIDNEY TRANSPLANTATION IN PATIENTS WITH IGA NEPHROPATHY: RECURRENCE RATE IN THE GRAFT AND LONG TERM OUTCOMES

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Background: To compare the long term outcomes of kidney transplant (KTx) recipients with IgA nephropathy (IgAN) as primary disease with those from a matched control group and also estimate the rate of IgAN recurrence in the graft.
Methods: We conducted a case control study, based on the data of our KTx registry, during the period 2000–2013. Inclusion criteria: Biopsy proven IgAN in the native kidneys and follow up longer than 1 year post KTx. Exclusion criteria: History of ABO incompatible KTx, major surgical complication during the first month, history of non-compliance. Patients and controls were matched for age, sex, donor source, year of KTx, and primary disease. Outcomes of interest were renal function at discharge, at 1st year and at end of follow up. We also estimated the rate of IgAN recurrence in the graft the related patient and graft survival in patients with and without IgAN recurrence.
Results: After exclusions, we identified 65 recipients with IgAN in the native kidneys, who were matched to a control group of 133 patients. GFR at 1st year and at end of follow up was shown similar between groups (p = 0.594). The incidence of acute rejection (AR) was 9.2% in the IgAN group versus 12.7% in the control group (p-value: 0.694). The rate of AR was higher in the control group (25.9×10^{-4} vs. 16.7×10^{-4} episodes/person-year). The incidence rate of IgAN recurrence was 10.4%. The mean time to recurrence was 39 months with a mean eGFR of 49.7 ml/min at the time of diagnosis and a mean proteinuria of 422 ± 419 mg/24 h.
Conclusion: In our cohort, long term outcome of KTx in patients with IgAN as primary disease was shown satisfactory. Graft survival and eGFR at 1st year and at end of follow up did not differ between cases and controls. IgaN recurrence in the graft was frequent, but not clinically significant in terms of long term graft function.

BO306

THE ASSESMENT OF LONG TERM OUTCOMES IN HBSAG NEGATIVE RENAL TRANSPLANT RECIPIENTS WHO WERE TRANSPLANTED FROM HBSAG POSITIVE DONORS

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Introduction: The aim of this study was to evaluate the long term outcomes of renal transplantation from HbsAg positive donors to HbsAg negative recipients.
Material and methods: A total of 78 patients who underwent renal transplantation in our clinic between January 2006 and May 2014 were included in the study. Patients were divided into two groups: Group 1: Donor HBsAg (+) ($n = 26$, HbsAb(-), HbeAg(-), HbeAb(+), HbcIgtotal(+) and HBV DNA (+), male/female (M/F):16 (61.5%)/10 (38.5%), Group 2: Donor HBsAg (-) ($n = 52$, M/F: 41 (78.8%)/11 (21.2%). HbsAb levels were similar in recipients of both groups. Data were collected retrospectively. Analyses were performed by using SPSS 20.0 software, patient and graft survival were measured by using Kaplan-Meier survival curve and compared by using log-rank test.
Results: Demographic datas were similar in two groups. The rate of acute Hepatitis B infection was significantly higher in Group 1 than Group 2 ($n = 3$, 11.5%; $n = 0$, 0%, respectively, p = 0.012). Acute hepatitis B attack were detected in vaccinated patients. Graft survival rates (groups 1–2 respectively; 1.-3.-5.-8. years: 95–96% / 95–94% / 85–88%/ 85–82%, p = 0.970) and patient survival rates (p = 0.098)(Figure 1)

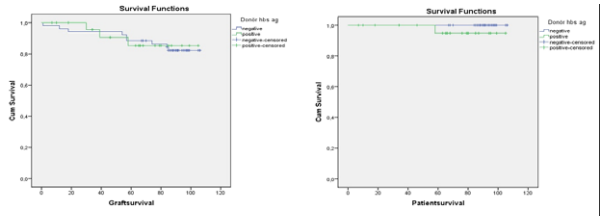

Figure 1. Graft and Patient survival rates for groups

, acute rejection rates (p = 0.725), delayed graft function, chronic allograft dysfunction, new onset diabetes after transplantation (NODAT), cytomegalovirus infection, the need for postoperative dialysis and plasmapheresis were similar between groups.
Conclusion: Our study revealed that the risk of developing acute hepatitis B was higher in patients which were renal transplanted from HbsAg(+) donors, but the other clinical outcomes were similar between groups.

BO307

LONG-TERM OUTCOMES OF SPOUSAL DONOR KIDNEY TRANSPLANTATION ACCORDING TO THE SPOUSAL RELATIONSHIP

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We investigated long-term clinical outcomes and risk factors in spousal kidney transplantation. Between July 1997 and December 2013, we performed 157 spousal donor renal transplants in our institution. Of those 157 spousal donor, 104 (66.2%) were female and 30 ABO incompatible grafts (19.1%) were included. According to spousal relationship, we divided into 2 groups: Group I: "wife-to-husband" ($n = 104$, 66.2%), Group II: "husband-to-wife" ($n = 53$, 33.8%). Graft survival rates at 1 year, 5 years, and 10 years post-transplantation were 97.1%, 91.5% and 87.8%, respectively, in the "wife-to-husband" group, 92.3%, 87.1% and 76.2%, respectively, in the "husband-to-wife" group. There were no significant differences between the two groups in graft survival (p = 0.368). The incidence of acute rejection (AR) episodes, surgical compli-

cation and infectious complication did not differ significantly. The delayed graft function (DGF) rates were significantly higher in patients with "husband–to-wife" group (18.9%, p = 0.021). The mean serum creatinine levels at 3, 5 and 7 year after KT were significantly lower in the "husband-to-wife" group, but serum creatinine level at 1 year and 2 years, did not differ significantly (p = 0.164 and 0.572, respectively). From Cox multivariate analysis, AR episode, DGF and Nephron mass index (kidney weight to recipient body weight ratio, Kw/Rw) were independent factors predicting the graft survival (OR 5.94, 4.55, 1.80, respectively) In our study, the graft survival rates between the two groups were not significantly different. Generally, the immunization of wife-recipients to their husband's HLA antigen by pregnancy attributes the higher DGF and AR episode, so it tends to have worse graft survival. However, the Kw/Rw ratio is an important factor of long-term graft survival and graft function. It offsets the immunologic negative factors for graft survals.

BO308 KIDNEY TRANSPLANTATION ALONE IN END-STAGE RENAL DISEASE PATIENTS WITH HEPATITIS B LIVER CIRRHOSIS

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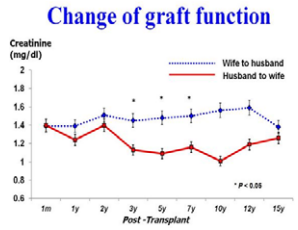
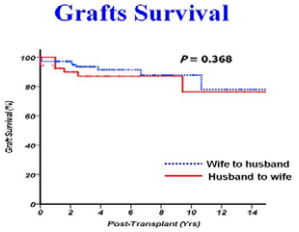
Background: Kidney transplantation (KT) alone in end-stage renal disease (ESRD) patients with hepatitis B virus liver cirrhosis (LC) is controversial. This study compared outcomes of KT in hepatitis B surface antigen-positive patients with ESRD with (LC group) and without LC (non-LC group).
Methods: Outcomes were analyzed in 116 hepatitis B surface antigen–positive patients with ESRD who underwent KT alone between 1997 and 2013 who were followed-up at least 1 year. Ninety-nine were in the non-LC group and 17 were in the LC group. Of the latter, twelve were Child-Pugh (CP) class A and five were CP class B.
Results: Baseline aspartate transaminase and alanine transaminase levels were higher in the LC group. Model for end-stage liver disease (MELD) scores were similar in patients with CP class A and class B, only serum albumin level was lower in CP class B. After KT, one CP class A patient showed an increase in the CP score from 5 to 10 points, MELD score from 22.3 to 44.1 points. The CP and MELD scores of the other 16 patients in the LC group did not increase. All five pre-KT CP class B patients were reclassified as class A after KT because of elevated serum albuminlevels. Four patients in the LC group developed hepatocellular carcinoma at a median of 35 months (range, 20–57 months) after KT. The 5-year patient survival rate was similar in the LC and non-LC groups. Occurrence of hepatocellular carcinoma was significantly higher in nonsurvivors than in survivors.
Conclusion: Kidney transplantation alone may be safe in patients with compensatedhepatitis B virus LC.





BO309 THE DIALYSIS SESSION DEPENDENT EFFECT OF DELAYED GRAFT FUNCTION ON GRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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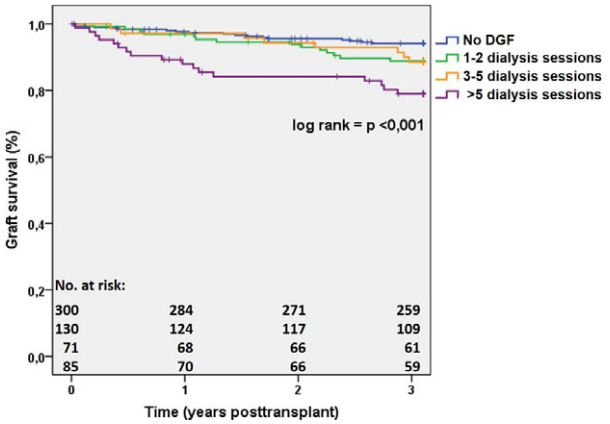
Delayed graft function (DGF), defined as dialysis within the first week after kidney transplantation, is a common risk factor for impaired graft function. So far the the impact of dialysis sessions on graft outcome in the long term is poorly evaluated.
Methods: In this retrospective observational study we analyzed a well-characterized cohort including 586 adult patients who received a deceased donor kidney over a period of 10 years. Demographics, clinical data and outcomes over a period of up to 3 years posttransplant were assessed. Mean follow up was 2.73 ± 0.71 years. For further analysis we created 4 groups who received 0, 1–2, 3–5 and >5 dialysis sessions, respectively. Analysis was performed by Kaplan-Meier survival curves (log-rank test) using SPSS. All results were censored for death.
Results: Among 586 recipients we found 286 (48.8%) who experienced DGF. After 3 years, in 13.6% patients with DGF graft loss occurred compared to 5.7% of patients without DGF (p = 0.001). Within the dialysis session groups patients with 1–2 (n = 130) and 3–5 dialysis (n = 71) no statistically significant difference in graft survival compared to patients without DGF was found. However, patients with >5 dialyses (n = 85) showed significantly increased numbers of graft loss (log rank p < 0.001) (Fig. 1). In the subgroup analysis of European Senior program patients (>65 years) >5 dialysis sessions (p = 0.009) showed significantly worse graft survival. Interestingly, in the group of 18–64 year old adults, representing the ETKAS group, significant results developed not until more than 10 dialysis sessions (p = 0.031) were performed.
Summary: DGF is a negative predictor for graft loss in a long term observational period of 3 years. Intriguingly, the performance of up to 5 posttransplant dialysis sessions does not seem to influence the occurrence of graft loss whereas the need of more than 5 dialysis markedly promotes graft loss. Moreover younger kidney recipients seem to preserve graft function despite prolonged delayed graft function.



BO310 DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANTATION – COMPARISON OF DIFFERENT DEFINITIONS AND 5-YEAR POSTTRANSPLANT OUTCOMES

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Background: Delayed graft function (DGF) traditionally is defined as requirement for dialysis within the first week after kidney transplantation, however there are also another definition proposed for this complication. The aim of this study was to compare different DGF definitions and impact on posttransplant results.
Methods/materials: Study included all consecutive cases of deceased donor kidney transplantation performed in one transplantation center between January 01, 2006, and December 31, 2007, where recipients were available for 5-year follow-up (101 transplantations, 66 deceased donors). Presence of DGF diagnosed based on traditional and 7 alternative DGF definitions (creatinine clearance, serum creatinine level, diuresis, need for dialysis, creatinine reduction ratio) [Daly et al., 2005]. We analyzed donor and recipient factors, associated with different DGF definitions, and 5-year posttransplant outcomes.
Results: Incidence of DGF according to traditional definition was observed in 20% of cases and showed significant variances in other definitions (from 6 to 54%). Analysis of associated factors revealed differences in associated factors: donor factors were associated with DGF in 7 of 8 definitions, recipient factors – in 4 definitions, sclerotic changes in donor kidneys revealed by „zero biopsies" – in 1 definition. Analysis of posttransplant results showed higher rate of acute rejections (observed in 7 DGF definitions), increase in posttransplant hospital stay (6 definitions), worse graft function at the end of follow-up (1 definition). Death-censored graft losses and patient deaths, as also 5-year graft survival did not show statistical association with any DGF definition.
Conclusions: Definitions showed different sensitivity to dynamical changes in kidney graft function with association with worse early posttransplant results, higher rate of acute rejections but less obvious impact on late posttransplant results.

025 LIVER

BO311 LEDIPASVIR/SOFOSBUVIR WITH RIBAVIRIN FOR THE TREATMENT OF FIBROSING CHOLESTATIC HEPATITIS C AFTER LIVER TRANSPLANTATION

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Background: Fibrosing cholestatic hepatitis (FCH) is a rare and severe form of recurrent hepatitis post liver transplantation with high morbidity (e.g., graft loss) and mortality. There are no approved treatments for FCH. This study evaluated ledipasvir/sofosbuvir (LDV/SOF) with ribavirin (RBV) in patients with biopsy-proven FCH.
Methods: In this open-label study, genotype 1 HCV-infected patients within 18 months of transplant, with histologic evidence of FCH (hepatocyte ballooning, periportal or pericellular/sinusoidal fibrosis, cholestasis, cholangiolar proliferation) total bilirubin $\geq 2.5\times$ ULN and no alternative explanations for cholestasis, were randomized to receive 12 or 24 weeks of LDV/SOF with RBV (weight-based). The primary endpoint is SVR12.
Results: 12 patients have been randomized and treated. Most were male (75%), Caucasian (83%), GT 1a (75%) and had prior HCV treatment (75%). Mean baseline HCV RNA was 6.8 log10 IU/ml [range 4.9–8.0 log10 IU/ml]. 9 patients have completed treatment and 3 are still receiving treatment. There have been no treatment discontinuations. 5 patients (42%) experienced treatment-emergent serious adverse events (SAEs). One SAE, dyspnea, was considered related to study treatment. The most common adverse events were anemia, headache, fatigue and pruritus. Laboratory values at baseline and Week 12 are presented in Table. Bilirubin, GGT and alkaline phosphatase (hallmarks of FCH), as well as albumin, platelets, ALT and INR were all improving with treatment by Week 12. By on-treatment week 4, eleven of 12 patients had HCV RNA < LLOQ and all 8 of the patients who have reached follow-up week 4 have achieved SVR4. SVR12 data will be presented.

		LDV/SOF+RBV ($N = 12$)	LDV/SOF+RBV ($N = 12$)
	Normal Ranges	Mean Baseline	Mean Week 12
Bilirubin mg/dL (range)	0.2–1.2	9.4 (1.5–28.1)	1.7 (0.6–5.2)
GGT, U/L (range)	4–61	554 (47–1332)	139 (15–686)
Alkaline phosphotase, U/L (range)	31–131	218 (114–562)	115 (40–356)
ALT IU/ml (range)	6–43	161 (62–220)	30 (8–100)
Hemoglobin g/dL (range)	11.5–18.1	12.5 (8.8–14.5)	11.6 (8.8–13.5)
Platelets $\times 10^3$ (range)	130–400	140 (40–217)	165 (53–280)
Albumin g/dL (range)	3.3–4.9	3.0 (2.2–3.8)	3.7 (2.7–4.6)
INR (range)	0.8–1.2	1.4 (0.9–3.6)	1.1 (0.9–1.3)

Conclusions: Administration of LDV/SOF+RBV in patients with FCH has been well tolerated and resulted in high SVR4 rates in a population with no other options.

BO312 OUTCOME OF LIVER TRANSPLANTATION IN WILSON DISEASE PATIENTS WITH NEUROPSYCHIATRIC MANIFESTATIONS

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[1]Shiraz University of Medical Sciences; [2]Gastroenterohepatology Research Center; [3]Shiraz Organ Transplantation Center

Background: Wilson disease (WD) is among the metabolic disorders that is cured by liver transplantation (LT). LT is indicated for WD in cases with medical treatment failure. There are defined indications for liver transplantation in patients with hepatic manifestations. However there is uncertainty about the role of liver transplantation and outcomes for WD patients with neuropsychiatric manifestations.
Material and Methods: All patients with the diagnosis of WD who received LT from 1989 to 2014 at Shiraz Organ Transplantation Center were included in the study. Patient's medical records were reviewed for pre-transplantation data. A detailed questionnaire for neuropsychiatric symptoms was obtained for each surviving patient by phone interview. The questionnaire included questions on the status of neurologic [?or psychiatric] manifestations of their WD.
Results: A total of 129 adult and pediatric liver transplantations were performed on patients with WD. The study group included 88 male and 41 females with a mean age of 21.46 $\pm$ 9.9 years. The clinical presentation of WD in 32 patients (24.8%) was hepatic without any neuropsychiatric symptoms or signs of disease (group A), and both hepatic and neuropsychiatric manifestations were initially present in 97 patients (75.2%) (group B). Nineteen patients (14.7%) presented with acute liver failure, all in the pediatric group. Five patients died, 1 in group A and 4 in group B, but the difference was not statistically significant. Pre-transplant neuropsychiatric manifestations in patients in group B were completely reversed in 49.5%, improved in 23.7%, unchanged in 19.6% and worsened in 7.2%. New neuropsychiatric manifestations developed in 19.5% of patients in group B and unexpectedly in 31.2% of patients in group A following LT.
Conclusion: Liver transplantation is lifesaving and effective for improving the neuropsychiatric manifestations of Wilson disease with good patient survival and outcomes. The course of neuropsychiatric manifestations due to WD is not predictable after LT and may dvelop even in the patients presenting with pure hepatic manifestations in their pre-transplant course. The presence of neuropsychiatric manifestation in non-debilitated forms should not be considered as a contraindication for LT in patients with WD.

BO313 SWITCHING FROM INTRAMUSCULAR OR INTRAVENOUS TO SUBCUTANEOUS HEPATITIS B IMMUNE GLOBULIN IMPROVES THE QUALITY OF LIFE OF LIVER TRANSPLANT RECIPIENTS

Riccardo Volpes[1], Patrizia Burra[2], Giacomo Germani[2], Paolo Strignano[3], Giorgia Rizza[3], Carla Migliaccio[4], Fulvio Calise[4], Mariarosa Tamé[5], Antonio Daniele Pinna[5], Matteo Manini[6], Lucio Caccamo[6], Paola Carrai[7], Paolo De Simone[7], Filippa Valentini Maria[8], Luigi Giovanni Lupo[8], Gabriella Cordone[9], Francesco Picciotto[9], Antonio Nicolucci[10]

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Background: After liver transplantation (LT), for prophylaxis of hepatitis B virus (HBV) reinfection, human hepatitis B immune globulins (HBIG) are administered by intravenous (IV) or intramuscular (IM) routes that differ for dosing, timing, schedules, and side effects, and can cause a negative impact on quality of life. A subcutaneous (SC) HBIG formulation has become available. Aim of the study was to evaluate the impact of switching from IM or IV to SC HBIG on the quality of life of LT recipients.
Methods/Materials: A longitudinal, prospective cohort of consenting adult LT patients was enrolled. All patients were administered the the SF-36 Health Survey and the Immunoglobulin Therapy After Liver Transplantation Questionnaire (ITaLi-Q) before and 24 weeks after switching from IM or IV to SC HBIG. The ITaLi-Q includes 37 items investigating 5 domains (side effects; positive/negative feelings; impact of HBIG on flexibility of daily activities; need for support; satisfaction). All scales are scored 0–100, with higher scores indicating a higher level on the measured dimension. Baseline and endpoint scores were compared by the Wilcoxon signed rank test.
Results: A cohort of 78 consenting patients was enrolled: mean age was 57 $\pm$ 10 years; 82% were males; 71% on IM and 29% on IV HBIG; mean interval from LT of 8 $\pm$ 6 years. Switching to SC HBIG was associated with significant improvements for the domains of side effects, negative feelings, flexibility, support, and satisfaction ($p < 0.0001$ for each scale). The SC route was associated with improvements in some SF-36 domains: role limitations for physical and emotional problems; bodily pain; social functioning ($p < 0.0001$ for each scale); the physical component summary score ($p = 0.001$), and the mental component summary score ($p = 0.006$).
Conclusions: Our study shows that SC HBIG improves the quality of life of LT recipients. This might in turn improve long term adherence to HBV prophylaxis, and needs to be explored in further studies.

BO314 HEALTH-RELATED QUALITY OF LIFE IS IMPROVED AFTER LIVER TRANSPLANTATION AND IS RELATED TO DISEASE ACCEPTANCE, HELPLESSNESS AND PERCEIVED DISEASE BENEFITS

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Ghent University Hospital

Background and Aims: Liver transplantation (LT) is the only curative treatment for end-stage liver disease (ESLD) with excellent long-term outcomes. However, an important outcome parameter is health-related quality of life (QoL). Improvement of QoL has been described after liver transplantation. We wanted to confirm these findings with specific attention for psychological parameters such as acceptance, helplessness and perceived disease benefits.
Methods: We performed a cross-sectional study in a liver transplant unit. Self-report questionnaires (SF36 and ICQ) were conducted in 177 patients with ESLD: 60 patients pre-transplantation, 60 post-transplantation and control group of 57 patients without perspective of transplantation. Data were analyzed using the Mann-Whitney U test and Spearman's rank correlation coefficient.
Results: The studied groups of patients were comparable regarding age and MELD score, but the control group was significantly older ($p < 0.0001$). We observed a significant increase in QoL as soon as 3 months after LT ($p = 0.046$) as well regarding the mental component summary scale ($p = 0.029$) as the physical component summary scale ($p = 0.033$). After liver transplantation, patients report more acceptance ($p = 0.001$) and disease benefits ($p < 0.0001$) and a decrease in helplessness ($p < 0.05$). General QoL is positively significant correlated ($p < 0.001$) with acceptance ($rs = 0.737$) and disease benefits ($rs = 0.494$), and negatively with helplessness ($rs = -0.828$).
Conclusions: These data confirm an increase of QoL starting from 3 months after liver transplantation. We observed a better acceptance of illness and more benefits of the illness after transplantation. Patients also report to feel less helpless. We assume that these findings indicate that patients receive a lot of attention and support for their illness after transplantation but still feel slightly uncertain. These aspects could give new directions in the approach of liver patients after transplantation.

BO315 ARTERY REPERFUSION FIRST WITH PORTO-CAVAL SHUNT IN DCD LIVER TRANSPLANTATION: IS IT A STRATEGY WORTH IMPLEMENTING?

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Background: DCD liver transplantation is frequently affected by intra-operative hemodynamic instability and initial graft dysfunction. Early reperfusion with arterialised blood under a temporary porto-caval shunt, with delayed portal reperfusion may be a benefit for livers from DCD. The aim was to explore differences in post-reperfusion syndrome (PRS) and the associated post transplant outcomes of grafts reperfused with the artery first (AR) compared to conventional portal venous reperfusion (PVR).
Methods: A total of 256 DCD liver transplants were performed in our unit since 2004. All DCD grafts undergone AR were compared with a matched cohort of PVR from March 2009 to October 2014. Matching was based on Donor Risk Index (DRI), donor WIT, recipient MELD and blinded to outcome. Donor, recipient and surgical characteristics between groups were compared and intra- and post-operative outcomes were analysed.
Results: A comparative analysis was performed on 20 matched pairs. There was no significant difference in donor and recipient characteristics between the AR and PVR groups. The AR group showed greater intra-operative stability compared with PVR: MAP 5 min after reperfusion was higher (81 mmHg vs. 69 mmHg, $p = 0.015$) and the incidence of post-reperfusion syndrome reduced (PRS) (0% vs. 22% $p = 0.034$)) with comparable requirements of inotropic support. There was a significant lower peak of bilirubin in the AR compared to the PVR group (78 vs. 130 mmol/l; $p = 0.017$). There was a lower trend of peak of postoperative transaminases and a higher trend of graft and patient survival at 3 and 12 months (90%vs. 84% and 90% vs.78%). The rates of postoperative renal failure, vascular and biliary complications were similar in both groups.
Conclusion: Artery reperfusion first in DCD liver transplantation can be a reliable strategy to have a better cardiovascular stability immediately after reperfusion and graft function with a trend of improvement in post-operative survival.

BO316 HEPATITIS B VIRUS-RELATED MIXED HEPATOCELLULAR-CHOLANGIOCARCINOMA IN PATIENTS UNDERGOING LIVER TRANSPLANTATION

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Yonsei University College of Medicine

Background: Mixed hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCC) is an uncommon form of liver cancer. As recent increase of liver transplantation (LT) for HCC, mixed HCC-CCC are increasingly being reported on pathological examination after LT. However, data on outcomes after LT for HCC-CCC are very limited. The purpose of present study was to analyze the tumor characteristics and post-transplant outcomes.
Methods: Patients with hepatitis B virus related mixed HCC-CCC undergoing liver transplantation at our institution between August 2006 and August 2014 were retrospectively analyzed.
Results: A total of 251 patients underwent LT for HCC. In the explant specimens of 10 of 251 patients (4.0%), HCC-CCC were identified (8 hepatitis B virus, 1 hepatitis C virus, and 1 alcoholic). Their median age was 53 years. Three patients underwent living donor and five patients underwent deceased donor LT. The median preoperative alpha-fetoprotein level was 12.9 ng/ml (range 1.9–178) and CA19-9 level was 31.4 U/ml (range 0.1–94). The median number of tumors was 2 and size was 2.75 cm. After a median follow-up period of 26.5 months, 3 of the 8 patients (37.5%) suffered from tumor recurrence. The sites of recurrence were intrahepatic ($n = 1$), lung ($n = 1$), and spine ($n = 1$). Overall patient survival at 1 and 3 years was 87.5% and 72.9%, respectively
Conclusion: Patients with hepatitis B virus-related mixed HCC-CCC are associated with a poor prognosis and a high rate of tumor recurrence after LT.

BO317 RESULTS OF 137 CONSECUTIVE LIVER TRANSPLANTATIONS WITH THE NEW COLD STORAGE SOLUTION SCOT 15

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Background: The new preservation solution SCOT15 contains 15 g/L of polyethylene glycol 20 kD which could decrease immunological recognition following reperfusion.
Methods/Materials: Among 300 cases, 137 human livers stored with SCOT15 were transplanted between 2009 and 2013.
Results: Main characteristics of the donor were: mean age: 52 ± 2 year, cold ischemic time: 7.8 ± 0.1 h, non or <30% steatotic graft: 97%. Main characteristics of the recipients were: MELD score 20 ± 1, main indication: cirrhosis (51%), hepatocellular carcinoma (36%) other (9%), retransplantation (reTx) (4%). Within 12 h following reperfusion a peak of transaminase release was observed (AST: 2211 ± 340 IU/L, ALT: 1222 ± 166 IU/L $n = 40$). In order to decrease it, from 2010 to 2013 during harvesting procedure the liver was flushed with 500 ml of NaCl 0.9% solution before using SCOT15 (AST. 1766 ± 232 IU/L ($p = 0.07$), ALT: 903 ± 96 IU/L ($p = 0.03$), $n = 97$). During day 6, total bilirubin was 87 ± 8 μmol/L and INR 1.25 ± 0.02. Excluding 4 grafts lost before day 6 (3 non-hepatic related deaths and 1 primary non-function from type 2 donation after cardiac death (DCD)) and according to Salvalaggio's criteria, early allograft dysfunction was absent in 68%, mild in 13%, moderate in 14% and severe in 5%. Rate of first arterial complication was 17/133 (13%), with 14 stenosis requiring stenting and 1 thrombosis. Rate of first biliary complication was 12/133 (9%), with 8 anastomotic strictures treated by endoscopic prosthesis and 3 supra-anastomotic strictures treated by prosthesis or late reTx. During follow up (median 27.4 months), reTx was needed in 6 cases (4%). Graft and patient survival were $88 \pm 3\%$ ($n = 119$) and $90 \pm 3\%$ ($n = 121$) at 1 year and $76 \pm 5\%$ ($n = 39$) and $80 \pm 4\%$ ($n = 42$) at 5 years, respectively. Excluding retransplantation, split liver, type 2 DCD and multiorgan transplant ($n = 112$) the 1 year graft survival was $91 \pm 3\%$ ($n = 100$).
Conclusion: SCOT15 is a valuable solution for liver transplantation.

BO318* PHYSICAL FITNESS BEFORE AND AFTER LIVER TRANSPLANTATION: A LONGITUDINAL STUDY

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Background: Physical fitness as assessed by maximal ergospirometry (VO2max, reflecting exercise capacity), 6 min walking distance (6MWD, reflecting functional exercise capacity), quadriceps force (QF) and handgrip force (HGF), is often impaired in patients with end-stage liver disease. We

Table 1. data expressed as median [IQR]; *p < 0.05 vs. PRE; *#p < 0.05 vs. POST; &p < 0.05 vs. 3M

	Pre	Post	3M	1Y
Exercise capacity (N = 26)				
VO_2max (ml/kg/min)	20.3 [14.6–24.4]	17.5 [12.9–22]	20.5 [13.9–24.5]	20.8 [17–27.8]#
VO_2max (%pred)	67 [53–88]	60 [48–77]	70 [55–81]	78 [63–98]#
Watt (%pred)	62 [42–88]	56 [34–67]*	65 [51–83]#	75 [56–94]#
6MWD (%pred) (*N* = 35)	73 [58–82]	67 [50–75]	82 [63–88]*#	83 [73–88]*#
Muscle force (N = 35)				
QF (*N*)	109 [84–147]	93 [72–130]*	123 [86–153]#	123 [97–161]#
QF (%pred)	73 [54–82]	67 [56–76]	75 [64–86]#	78 [63–87]#
HGF (*N*)	32 [22–39]	25 [19–36]*	30 [20–38]#	28 [21–40]#
HGF (%pred)	83 [70–107]	71 [52–93]*	74[61–102]#	83 [71–97]#
BMI	24 [22–28]	23 [20–28]*	24 [22–27]#	25 [23–28]#&

aimed to study the effect of Liver Transplantation (LTx) on physical fitness and body mass index (BMI).
Methods: 35 patients (age 53 ± 13 y, 18 male) were included. VO2max, 6MWD, QF and HGF were measured before LTx (PRE), 4–5 weeks postLTx (POST), 3 months after discharge (3M) and 1 year postLTx (1Y).
Results: Before LTx, VO2max, 6MWD and QF were severely impaired compared to the healthy population. Values tended to decrease at 4–5 weeks postLTx. After initial recovery at 3M, physical fitness no longer significantly increases and remains at approximately the same level as PRE LTx (except for 6MWD). BMI initially decreased postLTx but continued to rise at 3M and 1Y. (Table 1)
Conclusions: Physical fitness was impaired in LTx candidates. Although liver function normalizes after LTx, at 1Y physical fitness did not rise significantly above preLTx values. Whether pro-active rehabilitation programs and continuous counseling can accelerate/optimize physical recovery up to and beyond one year after LTx needs to be studied.

BO319

IMPROVEMENT OF SEXUAL FUNCTION IN MALE RECIPIENTS AFTER LIVING DONOR LIVER TRANSPLANTATION

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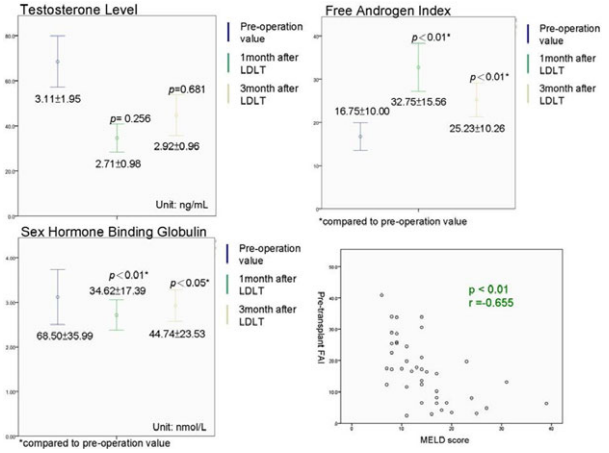
Background: Hypogonadism and sexual dysfunction are common clinical presentation in male liver transplant candidate. The aim of the study was to evaluate the effects of living donor liver transplantation (LDLT) on testosterone, sex hormone-binding globulin (SHBG), free androgen index (FAI) and erectile function in LDLT recipient.
Methods/Material: The Institutional Review Board at the Changhua Christian hospital approved the study. Male candidates for a LDLT were asked to participate in laboratory and questionnaire survey. Among the 43 eligible men, 41 (95%) completed the data collection during January 2014 to February 2015 in Changhua Christian Hospital, Changhua city, Taiwan. In the prospective study, serum levels of SHBG, and FAI of 41 male adult recipients were measured between 8 and 10 o'clock in the morning of the operation day and 1, 3 months after LDLT. The 5-item version of the International Index of Erectile Function (IIEF-5) Questionnaire was used before transplantation and six months after operation. Other clinical data were collected via chart review.
Results: SHBG level in the pre-transplant group was 68.49 ± 35.99 nmol/L and decreased to 34.62 ± 17.39 ($p < 0.01$) at 1 month, 44.74 ± 23.53 ($p < 0.01$) at 3 month after LDLT. FAI in the pre-transplant group was 16.75 ± 10.10. FAI increased to 32.75 ± 15.56 ($p < 0.01$) at 1 month and 25.23 ± 10.26 ($p < 0.01$) at 3 month after LDLT. The lower MELD Score (Model for End-Stage Liver Disease) was associated with worse pre-transplant testosterone level, FAI and better improvement of hormonal profile after transplant. The IIEF-5 scores significantly increased after LDLT (from 11.7 ± 7.7 before LDLT to 14.7 ± 7.5 after LDLT, $p < 0.01$).



Conclusions: Serum level of SHBG decreased and FAI increased after LDLT. The LDLT also results in improvement in erectile function. These data need further validation in larger trials.

BO320

WHICH IS THE PREDICTABLE VALUE OF POST-TRANSPLANT HCC RECURRENCE BETWEEN TUMOR-RELATED FACTORS AT THE INITIAL DIAGNOSIS AND THE TRANSPLANTATION?

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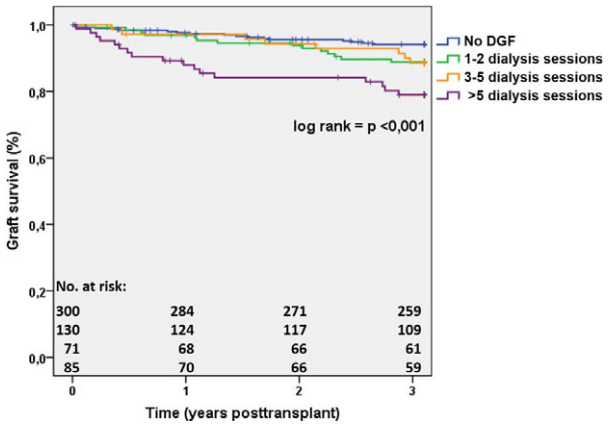
Background: Liver transplantation is treatment of choice about hepatocellular carcinoma (HCC). Though rapid improvements of surgical techniques, controls of tumor biology and immunosuppresants, recurrence of HCC remain of problem to overcome. Milan criteria is best options to decide whether patients with HCC underwent liver transplantation. However, Milan Criteria is not including values at time of fist diagnosis HCC. So it is not useful to apply of down staging, LT after resection, RFA or TACE. This study aimed to know Risk factor of recurrence of HCC at the time of not only liver transplantation but also first diagnosis.
Methods: Medical records of 228 liver recipients with HCC who underwent liver transplantation between Jan 2007 and Dec 2013 were retrospectively reviewed. The difference of disease free survival rate of above and Milan Criteria at the time of first diagnosis and liver transplantation were analyzed. AFP and PIVKA at that time were also analyzed.
Results: Among them, 191 Patients who underwent LT with HCC had no recurrence, however 37 patients had recurrence of HCC after LT. There were no significantly difference of gender, HBV, HCV, Donor type and Child- pugh score. In univariate analysis, Milan criteria at first diagnosis, Milan criteria at liver transplantation, AFP≥200 ng/ml at first diagnosis, AFP≥200 ng/ml at liver transplantation, PIVKA≥100 mAU/ml at first diagnosis and PIVKA≥100 mAU/ml at liver transplantation affected HCC recurrence. In multivariate analysis, AFP≥200 ng/ml at liver transplantation, PIVKA≥100 at liver transplantation and AFP≥200 ng/ml at first diagnosis affected disease free survival. (Hazards ratio 3.969, 3.002 and 2.459, respectively)
Conclusion: AFP, PIVKA at liver transplantation is strong risk factor of HCC recurrence. There are also poor prognosis factor that Patients have serum AFP level more than 200 ng/ml at first diagnosis HCC although within Milan criteria at liver transplantation.

Table 1. Multivaiate analysis

	Hazards Ratio	95% confidence interval	p value
AFP≥200 at liver transplantation	3.969	1.444–10.906	0.008
PIVKA≥100 at liver transplantation	3.002	1.313–6.863	0.009
AFP≥200 at first diagnosis	2.459	1.001–6.042	0.050



023 KIDNEY

BO321

IS CMV INFECTION A REAL RISK FACTOR FOR NEX ONSET DIABETES MELLITUS AFTER TRANSPLANTATION?

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Purpose: New-onset diabetes mellitus after transplantation (NODAT) is a well-known complication of transplantation. Patients with CMV infection had a lower median insulin release compared to their CMV negative counterparts, suggesting that impaired pancreatic β cell insulin release may be involved in the pathogenic mechanism of CMV-associated NODAT. Materials and Methods

We have been retrospectively evaluating CMV as a risk factor for NODAT in the set of 167 patients after kidney transplantation in the period of the first 12 months after kidney transplantation. We have excluded patients who were administered cyclosporine A or mTOR inhibitor. In each patient we have examined CMV viremia, by PCR in each month during the first 12 months after transplantation.

Results: There were 167 patients in the set, out of which 103 (61.7%) patients formed the control group and 64 (38.3%) patients formed the group with NODAT. Average level of tarcolimus (during the 12 monitored months from kidney transplantation) was without statistically significant difference

(p = 0.5592), similarly the average dose of prednisone/day (p = 0.0877). Average dose of mycophenolate mofetil/day or mycophenolate sodium was also without statistically significant difference (p = 0.0919 – MMF and p = 0.1734 – MPA). Average level of CMV viremia was without statistically significant difference (p = 0.9285). In the 10th month after kidney transplantation we have recorded significantly higher CMV viremia in the NODAT group (p < 0.0001), however, we have not proved this in the multivariate analysis. Thus, CMV has no relation with NODAT development in our set of patients during the monitored period. Patients' and graft survival 12 months after transplantation was without statistically significant.

Conclusion: In our analysis CMV is not a risk factor for NODAT. Results of the analysis (neither CMV nor NODAT development) are not distorted by the administered immunosuppression

	Control group *n* = 103	NODAT group *n* = 64	p value
average level of TAC (ng/ml))	4.7 ± 0.9	4.8 ± 1.2	0.5592
average dose of prednisone/day (mg)	8.2 ± 2.3	8.8 ± 2.0	0.0877
average dose of MMF/day (mg)	849.4 ± 264.2	911.7 ± 175.4	0.0919
average dose of mycophenolate sodium/day (mg)	670.7 ± 292	721.9 ± 113	0.1734
months after transplantation	control group (*n* = 103) CMV PCR (cop/ml)	NODAT group (*n* = 64) CMV PCR (cop/ml)	p value
1.	1177.1	0	0.3568
2.	6489.6	24241.9	0.3281
3.	26 346	4975.8	0.3080
4.	4578.9	6770.9	0.6551
5.	659.4	601.6	0.9007
6.	2729.2	270.9	0.2195
7.	52.1	2233.9	0.2138
8.	338.5	250	0.8397
9.	0	41.9	0.0858
10.	104.2	48256.6	<0.0001
11.	177.1	16.1	0.4674
12.	0	48.4	0.4382

Months after transplantation	Odds ratio	CI 95%	p value
1.	0.9990	0.6843–1.4582	0.9957
2.	1.0000	1.0000–1.0000	0.5884
3.	1.0000	1.0000–1.0000	0.1969
4.	1.0000	1.0000–1.0000	0.8043
5.	1.0001	0.9999–1.0003	0.3769
6.	0.9999	0.9998–1.0001	0.3515
7.	1.0000	0.9999–1.0001	0.5512
8.	0.9999	0.9994–1.0003	0.6266
9.	1.0210	0.0000–24969.8938	0.9968
10.	1.0000	1.0000–1.0001	0.6025
11.	0.9989	0.3234–3.0852	0.9985
12.	1.0066	0.0031–328.3802	0.9982

BO322 WAIST CIRCUMFERENCE AS AN INDEPENDENT RISK FACTOR FOR NEW ONSET DIABETES AFTER TRANSPLANTATION

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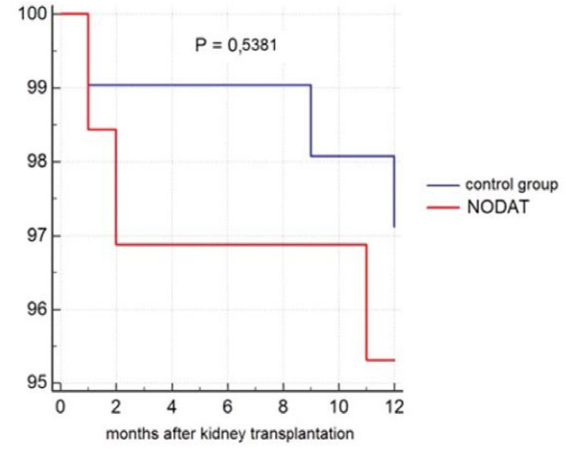
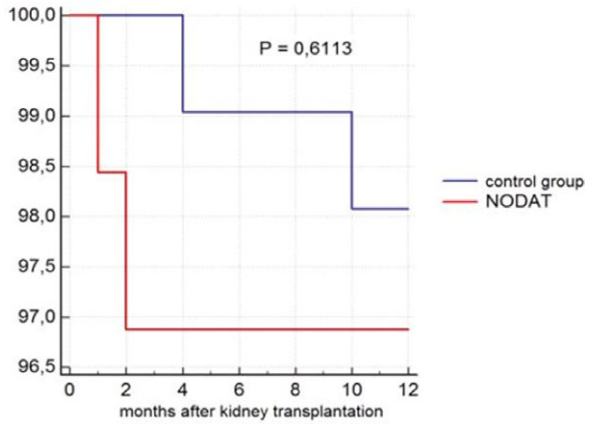
Purpose: New-onset diabetes mellitus after transplantation (NODAT) is a serious complication of solid organ transplantations. Visceral obesity is a key factor for diabetes mellitus type 2 and metabolic syndrome development and represents an independent risk factor for cardiovascular diseases.

Materials and methods: The set consisted of 210 patients (Europids) after primary kidney transplantation (90 patients had developed NODAT), average age of the set was 46.1 ± 11.6 years. We have retrospectively examined waist circumference (WC), body mass index and weight gain in the 12th month after transplantation. We have examined average level of triglycerides, cholesterol and immunosuppression throughout the 12 monitored months.

Results: Patients with NODAT were significantly older (p = 0.004),they had greater waist circumference (p < 0.0001) and higher average sirolimus level (p = 0.0262). We have identified following independent risk factors for NODAT: age at the time of transplantation higher than 50 years (HR = 2.5038, [95% CI: 1.7179 to 3.6492], p < 0.0001), WC in men greater than 94 cm (HR = 1.9492, [95% CI: 1.1697 to 3.2480], p < 0.0104), in women greater than 80 cm (HR = 4.5018, [95% CI: 1.8669 to 10.8553], p < 0.009). Greater WC related to higher incidence of NODAT (r = 0.1935, [95% CI: 0.01156 to 0.3630], p = 0.0374). 12-month graft survival (death censored) 12-month patient survival.





Conclusion: We have identified waist circumference as an independent risk factor for NODAT in our analysis. Waist circumference measuring is simple and accessible. Regular weight and waist circumference control in patients after kidney transplantation leads to identification of risk patients for NODAT.

BO323 RAISE OF BODY MASS INDEX AFTER RENAL TRANSPLANTATION

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Weight gaining is frequently encountered in patients after renal transplantation. Although it has many reasons, steroids, immunosupressive medications and resolving of chronical disease are mostly held responsible. Patients take more calories, according to change of eating habbits, especially by increased appetite and lower necessity for dietary restrictions. Overweighting is related to hypertension, dyslipidemia, and diabetes, as much as raise of mortality and morbidity due to cardiovascular diseases. The aim of this study is to determine the changes in body mass index of patients after renal transplantation.

The aim of this study is to determine the changes in body mass index (BMI) of patients after renal transplantation regarding to causes like steroid use, lower necessity for dietary restrictions, and changes in eating habbits. Ninety seven patients were enrolled to this retrospective study, who underwent cadaver or living donor renal transplantation between 2011 and 2013. Demographical features of patiens, heights and weights, body mass indexes were evaluated before and six and twelve months after surgery. The patients were grouped as malnutritioned, normal, overweighted and obese. Statistical analysis were

Results	Control group $n = 120$	NODAT group $n = 90$	p value
Age at the time of KT (years)	43 ± 11.3	52 ± 10	0.004
Weight gain 12 months after KT (kg)	6.5 ± 6.6	4.5 ± 5.7	0.1640
BMI value 12 months after KT (kg/m^2)	27.8 ± 4.8	29 ± 4.7	0.2617
Waist circumference 12 months after KT (cm)	99 ± 9.5	110.8 ± 12.9	< 0.0001
Waist circumference 12 months after KT (cm) – men	102.7 ± 9.4	107.6 ± 8	0.0007
Waist circumference 12 months after KT (cm) – women	92.8 ± 15.6	104.4 ± 11.3	< 0.0001
Triglycerides value (mmol/l)	2.0 ± 0.7	1.9 ± 0.8	0.5358
Cholesterol value (mmol/l)	4.4 ± 0.7	4.4 ± 0.8	1.000
% patients with tarcolimus (level)	85.6% (4.7 ng/ml)	84.6% (4.8 ng/ml)	0.5592
% patients with cyclosporine (level)	6.7% (86.9 ng/ml)	7.7% (9.6 ng/ml)	0.7804
% patients with mTOR inhibitors (level)	7.8% (5.8 ng/ml)	7.7% (7.6 ng/ml)	0.0262
Dose of prednisone (mg/day)	8.5 ± 2.3	8 ± 2.0	1.000
Results	Hazard ratio	CI 95%	p value
Age at the time of KT < 30 years	0.3065	0.08265–1.1363	0.0769
Age at the time of KT 31–39 years	0.5000	0.0526–4.7518	0.5714
Age at the time of KT 40–49 years	0.7000	0.4292–1.1416	0.1529
Age at the time of KT 50–59 years	2.5038	1.7179–3.6492	0.0034
Age at the time of KT ≥ 60 years	1.1376	1.0437–1.2399	< 0.0001
Waist circumference 12 months after KT ≥ 94 cm (men)	1.9492	1.1697–3.2480	0.0104
Waist circumference 12 months after KT ≥ 80 cm (women)	4.5018	1.8669–10.8553	0.009
Level of sirolimus < 6 ng/ml	0.2400	0.01467–3.9265	0.3169
Level of sirolimus ≥ 6 ng/ml	4.1667	0.2547–68.1682	0.3169

performed via SPSS 11.0 statistics program. Mean age of patiens was 38.9 ± 12.1 years. 26.19% were female, 73.81% were male. Mean body mass index before surgery was 22.52 ± 3.97 kg/m^2. Post transplant after six months mean BMI was 24.40 ± 4.1 kg/m^2 and after 12 months it was 25.56 ± 4.14 kg/m^2 ($p < 0.05$). 68% of patients showed improvement after 12 months of surgery, who were in the preoperative malnutrition group. There is significant raise in the BMI of patients in the first year, who undergo renal transplantation, and the reason is mulifactorial. BMI is relevant to diabetes, hypertension and allograft nephropathy. BMI should be carefully considered in the follow up of patients who underwent renal transplantation, and early nutritional changes with dietary and exercise programmes should be performed in overweighted cases.

	Pretransplantation	6th month	12th month
BMI (kg/m^2)	22.52 ± 3.97	24.4 ± 4.1	25.56 ± 4.14
MDRD eGFR (ml/min/1.73 m^2)		55.6 ± 18.1	54 ± 15
Least BMI (kg/m^2)	16	18.2	19
Highest BMI (kg/m^2)	34.3	35.6	35.8

BO324* APELIN AND NEW ONSET DIABETES AFTER TRANSPLANTATION IN LIVING KIDNEY ALLO GRAFT RECIPIENTS

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Objectives: Apelin, a cytokine mainly secreted by adipocytes and a variety of tissues, including gastrointestinal tract, adipose, brain, kidney, liver, lung and various sites within the cardiovascular system. Apelin is closely related to glucose metabolism and was proposed to be a promising therapeutic agent for treating insulin resistance. Apelin and orphaned G-protein – coupled apelin (APJ) exhibit roles in the regulation of fluid homeostasis. Circulating serum apelin suppresses insulin secretion by binding to the APJ receptor on B cells of islets of Langerhans. Several studies have also documented the altered level of serum apelin in type 2 diabetic patients, but the results remain controversial. The purpose of this study was to analyze apelin levels in new onset diabetes after transplantation (NODAT). Material and method

Forty seven diabetic renal transplant recipients were compared to forty non diabetic renal transplant recipients. Positive family history of diabetes, body weight, BMI, blood pressure, blood chemistry, including apelin level. Logistic multiple analysis were made for statistically significant data on univariate analysis.

Results: Apelin levels were significantly higher among obese, hypercholesterolemia NODAT patients, 428.7 ± 193.29, 256.8 ± 128 ($p > 0.001$). There was appositive correlation between serum apelin and Proteinuria.

Conclusion: Serum Apelin has a high level in NODAT Patients than non-diabetic patients and positively correlate with proteiurea in NODAT Patients.

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BO325 THE RISK FACTORS FOR BONE DISORDER AFTER RENAL TRANSPLANTATION

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Background: In light of greatly improved long-term patient and graft survival, improving other clinical outcomes after renal transplantation such as risk of fracture is of paramount importance. However, the parameters influencing bone health in Chinese patients have not been well defined in its pathogenesis.
Methods: A total of 124 recipients who underwent living-related donor renal transplantation between 2007 and 2011 at West China Hospital of Sichuan University were included. Dual-energy X-ray absorptiometry was performed to measure BMD. Patients were divided into two groups according to BMD results: group 1 with normal bone mineral density (T score above −1.5), group 2 with low bone mineral density (T score below −1.5). Clinical information such as sex, age, types of immunosuppressive drug and time since transplantation were included. Laboratory tests for parameters included serum blood urea nitrogen, creatinine, uric acid, Cystatin C, calcium, phosphorus,parathyroid

hormone,25-hydroxy vitamin D, bone-specific alkaline phosphatase, tartrate-resistant acid phosphatase-5b levels. Statistical analyses were performed using non-conditional logistic regression analysis to assess the effects of the different parameters to find possible risk factors and main factors.
Results: Of 124 patients, 14.5% had low bone mass in Lumbar vertebrae L1–L4. Non-conditional logistic regression analysis revealed that BMI seemed to be preventative for bone loss after transplantation ($p = 0.029$, OR = 0.591, 95%CI = 0.369~0.947). 31.5% had bone loss in the neck of the femur, and low BMI, high Cystatin C seemed to be the risk factors in this part of skeleton (Cystatin C: $p = 0.007$,OR = 25.127, 95%CI = 2.403~262.776; BMI: $p = 0.012$, OR = 0.736, 95%CI = 0.580~0.935).
Conclusion: Disturbances in bone metabolism are common complications after renal transplantation, which requires detection and treatment to reduce fracture incidence. Low BMI and highCystatin C were found to be main risk factors in our study.

BO326 EZETIMIBE/SIMVASTATIN USE IN KIDNEY TRANSPLANT PATIENTS

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Backgroud: The objective of this study was (1) to assess the consistency of effect of the combination Ezetimibe/Simvastatin (Inegy) in kidney transplant patients after a switch from statins and (2) to assess its safety and tolerability.
Material/Methods: This was a prospective observational study over 6 months. Patients with uncontrolled cholesterol level on statins alone for at least 6 months and stable eGFR above 60 ml/min/1.73 m^2 were eligible for switching to Inegy 10/40. Percent change of lipids was assessed between the start (time 0), at 3 and 6 months of treatment. Safety, tolerability and the effects on kidney function, cyclosporine levels and liver function were evaluated.
Results: Eighteen patients (10 males and 11 diabetic) all on cyclosporine finished the study. The mean age was 54.4y (39–70). The mean post-transplant period was 8.05y (2–13). The patients were on Atorvastatin 40 mg ($n = 8$), Fluvastatine XL 80 mg ($n = 4$) and Atorvastatin 20 mg ($n = 6$). After 6 months on Inegy, the total cholesterol percent change was 24.50% less, as well as ldl-cholesterol (24.63%) and triglycerides (34.64%). However we noticed a negative percent change in hdl-cholesterol (12.19%). Serum creatinin measurements and blood levels of cyclosporine were stable all through the study period for all the patients and no adjustments of cyclosporine doses were required. Two patients complained of myalgia which was moderate, not associated with elevated CK and did not lead to Inegy discontinuation. No major abnormalities were noticed in the liver function tests. Tolerability of Inegy was overall acceptable.
Conclusion: This short term study showed that the combination Ezetimibe/Simvastatin use in kidney transplant patients was efficient in reducing total cholesterol, LDL cholesterol and triglycerides. It showed also that tolerability and safety were above expectations. Long term studies are needed to assess sustainability of these results.

BO327 A CHANGE IN INSULIN SENSITIVITY AND LIPID PROFILE IN RENAL TRANSPLANT RECIPIENTS CONVERTED FROM CYCLOSPORINE OR STANDARD RELEASE TACROLIMUS TO ONCE-DAILY PROLONGED RELEASE TACROLIMUS

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Background: New-onset diabetes after transplantation may be associated with the use of tacrolimus (Tac) causing impaired insulin release or reduced insulin sensitivity. And, dyslipidemia commonly occurred after transplantation. Such effects in insulin sensitivity and lipid profile have not been studied in renal transplant recipients receiving traditional twice-daily tacrolimus (TacBID) or cyclosporine and then compared to the new once-daily prolonged release formulation of tacrolimus (TacOD).
Methods: We performed an observational prospective study of 20 stable non-diabetic renal transplant recipients on change in insulin sensitivity and lipid profile in renal transplant recipients converted from cyclosporine or standard release tacrolimus to once-daily prolonged release tacrolimus. We evaluated the level of HbA1c, total cholesterol, HDL, LDL, TG, apolipoprotein A1, apolipoprotein B, serum creatinine, fasting plasma glucose, fasting insulin and HOMA-β at base line, two and four months. To analyze differences in parameter, we performed a t-test in both groups (cyclosporine to TacOD conversion group/TacBID to TacOD conversion group).
Results: Tacrolimus trough concentration was 4.5 ± 0.5 μg/ml. The result did not showed and any change in insulin sensitivity and lipid profile after conversion at two and four months.
Conclusion: Conversion from standard TacBID or cyclosporine to TacOD is safe. In spite of a reduced Tac exposure, there was no change in insulin sensitivity and lipid profile in renal transplant recipients.

BO328 ASSOCIATION OF GENETIC POLYMORPHISMS OF MATRIX METALLOPROTEINASES WITH NEW-ONSET DIABETES AFTER TRANSPLANTATION IN RENAL TRANSPLANTATION

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Background: New-Onset Diabetes After Transplantation (NODAT) is a serious metabolic complication that may follow renal transplantation. Excess fat deposition requires space, created by adipocyte (hypertrophy and hyperplasia) and extracellular matrix (ECM) remodelling. This process is regulated by several factors, including several adipocyte-derived Matrix metalloproteinases (MMPs) and the adipokine cathepsin, which degrades fibronectin, a key ECM protein. Excess fat, also deposited in visceral organs, generates chronic low-grade inflammation that eventually triggers insulin resistance and the associated diabetes mellitus. Therefore, we examined the association between NODAT and 11 single nucleotide polymorphisms (SNPs) located within the 3 genes of Matrix metalloproteinases (MMPs) which might be related with NODAT.
Methods: A total of 309 renal transplants recipients were included without a history of diabetes. We analyzed the association between NODAT development and a panel of 11 SNPs within 3 genes (MMP1, MMP2, MMP3) of MMPs.
Results: In terms of allele frequencies, rs243849*C (MMP2) was significantly higher in patients with NODAT. Two SNPs among 11 (18.1%) were significantly associated with NODAT development after adjusting for age, sex, and tacrolimus usage. They include MMP2 (rs1132896) and MMP2 (rs243849). In multiple logistic regression analysis, these 2 SNPs were significantly associated with the development of NODAT in the codominant and recessive or, codominant and dominant models, respectively.
Conclusions: The data suggest that excess fat deposition and ECM remodelling might play a role in the pathogenesis of NODAT in renal transplantation recipients. In particular, significant variations of MMP2 might confer susceptibility to NODAT in patients who receive renal transplants.

BO329 THE IMPACT OF TRANSIENT POST-TRANSPLANT HYPERGLYCEMIA IN KIDNEY TRANSPLANT RECIPIENTS ON TRANSPLANT OUTCOMES

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Background: Hyperglycemia occurs frequently after kidney transplantation and may be reversed when the dosage of the immunosuppressive agents is tapered. However, the effect of transient post-transplant hyperglycemia (PTH) on transplant outcomes is not well described.
Methods: Kidney transplant recipients (KTRs) without diabetes were enrolled in the study. Transient PTH was defined as recovery from PTH without further antidiabetic therapy and the maintenance of glycated hemoglobin levels <6.5% at 1 year after transplantation. Persistent PTH until 1 year after transplantation was considered as new-onset diabetes after transplantation (NODAT). We analyzed the factors associated with increased risk of PTH and compared the development of diabetes mellitus, cardiovascular disease, and other transplant outcomes among no PTH, transient PTH and NODAT groups.
Results: Among 176 KTRs, 106 (60.2%) developed PTH and 58 (54.7%) of 106 patients with PTH had transient PTH. Transient PTH and NODAT groups showed significantly higher average daily glucose levels than no PTH group from the first post-transplant day. Old age, high body mass index (BMI), and female gender were independent risk factors for transient PTH. The incidence of diabetes was not significantly different between patients with no PTH and those with transient PTH. The incidence of cardiovascular disease was significantly increased in NODAT group compared with that in no PTH and transient PTH groups. However, the incidences of acute rejection, allograft loss, and patient death were comparable among three groups.
Conclusions: Transient hyperglycemia in KTRs appeared at the immediate post-transplant period and was associated with old age, high BMI, and female gender. However, transient elevation of blood glucose level did not affect post-transplant outcomes, including diabetes mellitus and cardiovascular disease. In contrast, patients with NODAT should be carefully monitored for the occurrence of cardiovascular disease.

BO330 PREVALENCE OF METABOLIC SYNDROME IN RENAL TRANSPLANT PATIENTS: ROLE. EARLY ASSESSMENT

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Metabolic Syndrome (MS) is now recognized as a risk factor for Cardiovascular (CV) disease, the leading cause of death with a functioning graft in renal transplantation. This study evalued the prevalence of MS in final first year post renal transplant. From 376 adult patients renal transplanted from 2012 to 2013 we invited 121 patients to perform a cross-sectional study evaluating all MS risk factors according to the International Diabetes Federation (IDF) in final first year post renal transplant. Three patients were excluded due to no agreement, BMI 40 kg/m^2 or GFR 20 ml/min. Our study population consisted of 118 patients,(pts) female (54%), white (64%), with mean age4111 years. Mean SCr was1,691,06 mg/dL and mean eGFR (MDRD)52 $\pm$ 23 ml/min/1.73 m^2. Mean BMI was29.8 $\pm$ 5 kg/m^2. All pts were under steroids and 98 in use of calcineurin inhibitors. Eleven patients (9%) were new-onset diabetes post transplant. From all risk factors for MS, hypertension was present in 77 (65%), low HDL in 73 (63%), hypertriglyceridemia in 49 (41%), large waist circumference in 34 (29%), hyperglicemia in 30 (25%) pts. MS (3 risk factors) was observed in 52 (44%)pts. 36 (48%) pts had 3 risk factors and only 4 pts (3%) had all risk factors. There was a predominance of young pts (age<50 years) with good renal function (SCr<2.0 mg/dL) among pts with MS compared to without MS (age<50 years:MS 62% vs. no MS 38%, $p < 0.0001$; SCr <2.0 mg/dL: MS 47% vs. no MS 53%, $p = 0.03$). Analising all pts, we observed mean BMI among pts with MS was major (BMI = 31.4 $\pm$ 4.4) compared to patients without MS (BMI = 28.1 $\pm$ 4.8)($p < 0.001$). Others risk factors for CV not SM also was present in patients with MS compared to without MS (Mean Insulin 16.8 $\pm$ 12.8 vs. 10.3 $\pm$ 1.4 $p < 0.001$; Mean HOMA 4.3 $\pm$ 3.7 vs. 2.4 $\pm$ 2.1, $p < 0.001$; Mean Hemoglobin a1c5.7 $\pm$ 0.6 vs. 5.4 $\pm$ 0.7,$p < 0.001$). In our renal transplanted population, MS is already present in the first year and others and others risk factors for CV no SM also should also be considered.

BO331* DONOR-SPECIFIC ANTIBODY RATES ACROSS 7 YEARS OF TREATMENT WITH BELATACEPT: FINAL RESULTS FROM BENEFIT

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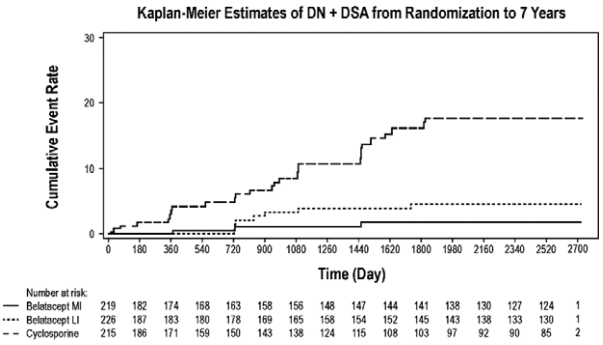
Purpose: The presence of donor-specific antibodies (DSA) has been associated with an increased risk of antibody-mediated rejection and graft failure. De novo (DN) DSA specific to Class II HLA are associated with worse prognosis than those specific to Class I. Prior analysis of the BENEFIT trial demonstrated lower rates of DN DSA in the belatacept (bela) vs. CsA arms at 3 years in the intent-to-treat population and at 5 years in the long-term extension population. We report herein the DN DSA rates from baseline through Year 7 (final data point) in BENEFIT.
Methods: Recipients of living donor or standard criteria donor kidneys were randomized to bela MI or LI or CsA treatment regimens. DN DSA rates were assessed for all randomized and treated patients from baseline through Year 7. The presence of DSA was established centrally by solid phase flow cytometry (FLowPRA™). Specificity (Class I and II) was assessed by LabScreen™ single antigen beads (One Lambda, Inc.). Kaplan-Meier estimates for the cumulative rate of development of DN DSA from randomization to study end were derived.
Results: In total, 666 pts were randomized and transplanted (bela MI, $n = 219$; bela LI, $n = 226$; CsA, $n = 221$). The cumulative event rates of DN DSA at Years 3, 5, and 7 for bela MI were 1.18, 1.86, and 1.86, respectively. The corresponding values for bela LI were 3.40, 4.64, and 4.64. The cumulative event rates at Years 3, 5, and 7 for CsA were 8.72, 16.19, and 17.81, respectively. DN DSA Class I HLA specificity was found in 1 MI-treated, 3 LI-treated, and 7 CsA-treated patients. Class II HLA specificity was found in 2 MI-treated, 4 LI-treated, and 14 CsA-treated patients. Both Class I and II HLA specificity was observed in 4 patients receiving CsA.
Conclusions: Data from BENEFIT demonstrate a reduced incidence of DN DSA with bela (MI or LI) vs. CsA across 7 years of treatment. Further study is required to determine if the reduced incidence of DN DSA leads to better long-term outcomes.



BO332* MALIGNANCIES AFTER KIDNEY TRANSPLANTATION ARE ASSOCIATED WITH AN INCREASED RISK OF GRAFT LOSS BUT NOT OF CHRONIC REJECTION

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Introduction: Studies on the role of malignancies on kidney graft survival are lacking: we retrospectively analyzed the impact of non-melanoma skin cancer (NMSC) and non-cutaneous malignancies (NCM) on death-censored graft survival with a time-dependent multivariable Cox model, adjusted by known prognostic factors.
Population: We included 682 consecutive adult patients receiving their first kidney transplant from a deceased donor, with at least six months of follow-up (male: 426/682 = 62.5%; median age: 53 years).
Results: During a median follow-up of 4.65 years, 63 patients lost their graft function; 50 patients developed a NMSC (10-years incidence: 11.1%), and 41patients developed a NCM (10-years incidence: 9.1%). In the multivariable model, NMSC were not associated with graft loss (HR = 0.78; 95%CI = 0.29–2.07, $p = 0.62$), while NCM were associated with a significant HR of 2.69 (95% CI = 1.17–6.18, $p = 0.02$; see Table). After a NCM, graft survival was 65.5% at 5 years. When stratifying for graft loss causes, NCM was not associated with graft loss caused by chronic rejection (HR = 0.98; 95%CI = 0.22–4.48, $p = 0.98$), but it was strongly associated with other causes (HR = 8.18; 95% CI = 2.77–24.2, $p < 0.01$). Graft failure in patients with a NCM was not associated with IS therapy reduction (HR = 0.82; $p = 0.79$), surgery (HR = 0.59; $p = 0.45$), chemotherapy (HR = 0.72; $p = 0.66$) or radiation therapy (HR = 0.39; $p = 0.37$).
Conclusions: This is the first study comparing graft survival in patients with and without a post-transplant malignancy: patients with a NCM are at increased risk of graft failure, particularly other causes than chronic rejection. Therefore more efforts should be made to improve graft outcomes after a NCM, particularly acting on malignancy-associated nephropathies.

Risk Factor	HR	95%CI	p
Non cutaneous malignancy	2.69	1.17–6.18	0.020
pCreat at 6 months > 2 mg/dL	3.16	1.74–5.73	<0.001
U-prot at 6 months > 0.5 g/24 h	2.30	1.31–4.03	<0.001
Acute rejection	3.27	1.71–6.26	<0.001
Donor age (10-years increase)	1.22	1.05–1.48	0.019

BO333* OUTCOME ON RENAL FUNCTION, EFFICACY AND SAFETY IN LIVING-DONOR KIDNEY TRANSPLANT RECIPIENTS AFTER CONVERSION FROM CNI TO EVEROLIMUS-BASED REGIMEN: 5 YEAR DATA *POST HOC* ANALYSIS FROM THE ZEUS STUDY

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Background: To study renal function and patient outcome after 5 years in living donation subgroup of kidney *de novo* transplant (Tx) recipients after conversion to an everolimus (EVR)-based regimen and withdrawal of calcineurin inhibitor (CNI) therapy.

Methods: *Post hoc* subgroup analysis from the prospective, open-label, controlled, multi-centre study ZEUS. 300 kidney Tx patients were randomised at month (Mo) 4.5 post Tx to either receive EVR plus enteric coated-mycophenolate sodium (EC-MPS) or cyclosporine (CsA) plus EC-MPS regimen, among them 80 were living donor (LD) recipients (EVR group $n = 42$; CsA group $n = 38$). Observational follow-up (FU) on pts safety and efficacy was done until Mo60 post Tx.
Results: Adjusted estimated glomerular filtration rate (eGFR; Nankivell) in living donation subpopulation at Mo60 was 67.0 (95% CI [62.2; 71.9]) ml/min/1.73 m^2 in EVR vs. 60.5 (95% CI [55.2; 65.7]) ml/min/1.73 m^2 in CsA pts, resulting in a difference of +6.6 ml/min/1.73 m^2 in favour of EVR pts ($p < 0.01$). Unadjusted mean eGFR at Mo60 was 69.5 ml/min for EVR vs. 60.6 ml/min for CsA ($p = 0.03$). BPARs during FU after Mo12 occurred in 4 pts of the EVR and 3 of the CsA group, all BANFF grade IA except one BANFF grade IIA among EVR pts. From randomisation to Mo60 one death occurred in CsA living donor recipients, two in the EVR living donation subgroup; one graft loss occurred in the EVR, none in the CsA group. Overall safety profile was similar between both treatment groups.
Conclusions: The presented analysis shows that EVR-based regimen with early elimination of CNI therapy in living donor kidney Tx recipients is associated with a significant benefit on renal function maintained for 60Mo post Tx without compromising safety and efficacy.

BO334*

DONORS WITH STONE-BEARING KIDNEYS ARE ELIGIBLE FOR LIVING KIDNEY DONATION: A SYSTEMATIC REVIEW AND COHORT ANALYSIS

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Background: Since living kidney donation can still not meet the demand for donor organs, extended criteria donors are increasingly included, such as donors with one or more kidney stones. Little is known about the outcome of these donors, as a possible future risk exists that recurrent stones, obstructions, and infections could injure the remaining kidney. Furthermore, the outcome of renal transplant recipients that retrieve a kidney with stones is of great importance as inadvertent transplantation could also impair recipient outcome.
Methods: Comprehensive searches were carried out in several databases up to December 2014 to search for relevant articles. We evaluated current guidelines for donors with stone disease and data to review to which extend stone-bearing kidneys are eligible for living kidney donation. Furthermore, the cohort of 1555 donor nephrectomies and transplantations in the center of the authors was analysed for outcome of donors and their recipients.
Results: Of the 3115 articles found, 18 met the inclusion criteria. Based on the literature search, both in attitude and in practice there is a shift in accepting more donors with (a history of) kidney stones. The prevalence in the literature ranges from 0.6% to 7%. In our cohort, the prevalence of kidney stones was 2.3% (36 live kidney donors). 21 donations of stone-bearing kidneys took place, of which 3 donors developed a stone-related event, which all passed without intervention. Three of the recipients developed a stone-related complication, which were all successfully treated.
Conclusion: We conclude that asymptomatic stone-bearing kidneys seem to be suitable for donation and transplantation. Both donors and recipients have excellent outcome. However, a sufficient follow-up is required to confirm these outcomes in the long-term. We would advice that current guidelines are revised to remove stone-bearing kidneys as an absolute contra-indication for donation and transplantation.

BO335

ACCESS TO RENAL TRANSPLANTATION IN DENMARK

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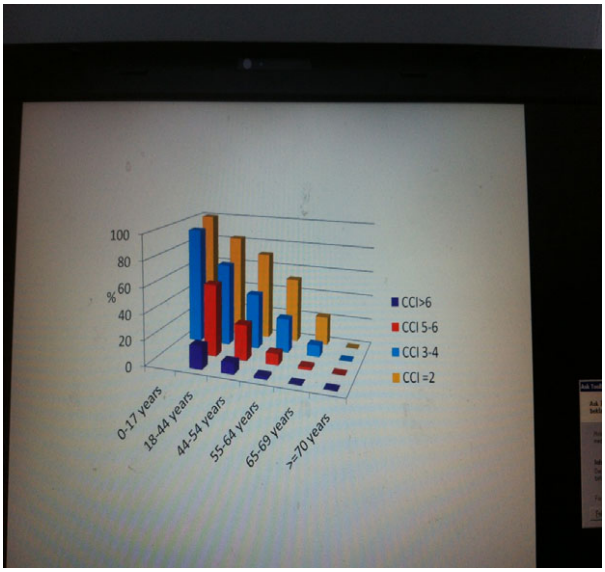
Background: The survival benefit of renal transplantation has been demonstrated in several studies. However, only a limited proportion of patients with end- stage renal disease (ESRD) are eligible for transplantation. We aimed to analyse access to transplantation in different patient groups with ESRD.
Methods and materials: Data from the Danish Nephrology Registry and Scandiatransplant were merged. Charlson Co-morbidity Index (CCI) scores were derived from the National Danish Admissions Registry, which records all discharge diagnoses. Study period was 01.01.2004 to 31.12.2011. All patients, who started treatment for ESRD during the first 5 years of the study period, were included and all patients were followed for 3 years. Access to transplantation was defined as either waitlisting or performed renal transplantation within 3 years after starting treatment for ESRD. Patients were divided according to age- group and CCI score.
Results: A total of 3563 patients with ESRD were included. 804 patients (23%) were given access to transplantation (on the waiting list or transplanted) within the first 3 years after starting treatment for ESRD. Of these, 67.5% (543 patients) had a renal transplant within 3 years. Access to transplantation in different age-groups was: patients 0–17 years:98%, 18–44 years: 73%, 45–54 years: 48%, 55–64 years: 25%, 65–69 years: 10%, ≥ 70 years: 0.3%. Among patients < 18 years only 1 patients had CCI > 4 and this patient is not shown in the figure 1 due to small number in the category.
Conclusion: As expected, access to transplantation decreased by increasing age and increasing CCI score. Especially among patients older than 45 years a high CCI score was associated with low rate of access to transplantation. Patients older than 70 years counts for 40% of incident patients with ESRD in Denmark but less than 1% of these patients were waitlisted.



BO336

A COMPARISON OF TRANSPLANT OUTCOMES IN PERITONEAL AND HEMODIALYSIS PATIENTS

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Introduction: The majority of patients referred to transplantation are on hemodialysis or peritoneal dialysisThe pre-transplant dialysis modality might influence transplant outcome.
Methods: We analyzed the effect of pre-transplant dialysis modality on transplantation outcomeTo minimize the donor variability and bias,a paired kidney analysis was applied. Observation lasting 20 years included 185PD patients from our unit. PD constituted 13.3%of all patients transplanted during that period.133PD patients had HD pairs receiving grafts from the same donor. In 52other cases both patients were on PD and either graft was from a living donor or a pair received preemptive transplant,or only one kidney was transplanted
Results: PD patients were slightly younger (46.5 vs. 48.7 years)and had significantly shorter renal replacement therapy time (23 vs. 35 months) ($p < 0.05$). Primary glomerulonephritis was the most common cause ESRD in both groups (34%). Charlson Comorbidity Index was (2.68 vs. 2.54)For 5PD, and 9HD,patients it was the second or the third transplantation. The groups did not differ significantly with respect to type of immunosuppressive protocol and number of mismatches.60% of donors had traumatic cause of death,mean eGFR was 107 ml/min/1.73 m^2)One year patient (96 vs. 100%)and graft (93 vs. 97%)survival were similar in boths groups respectively. DGF occurred significantly more often in HD recipients (15 vs. 37%)($p < 0.05$)but more PD patients experienced infections (31 vs. 28%)Graft vessels thrombosis resulting in graft loss occurred in 8PD6% and in 2HD1.5% patients ($p < 0.05$)Creatinine and eGFRone year and three years after transplantation did not differ (1.18 vs. 1.21;1.17 vs. 1.25 mg/dl)Acute rejection (not always biopsy proven)was observed significantly more frequently in HD patients (13 vs. 22%)($p < 0.05$)
Conclusion: Long term outcome of renal transplantation is similar in patients coming from either PDorHD. PD patients experience significantly less DGF and AR but significantly higher risk of graft vessels thrombosis

BO337 THE EFFECT OF INTERVAL BETWEEN KIDNEY TRANSPLANTATION AND PREGNANCY IN GRAFT SURVIVAL

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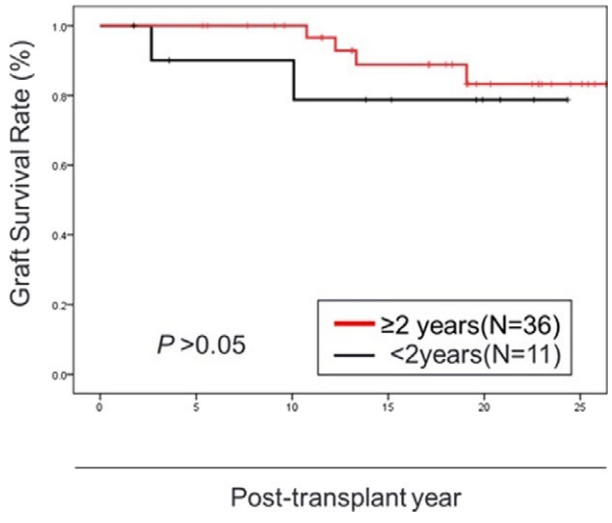
Background: Successful kidney transplantation (KT) makes the recipient who infertile could become pregnant. When we plan the pregnancy in childbearing woman undergone KT, we consider many qualification such as adequate immunosuppression, stable serum creatinine concentration, no proteinuria, and well controlled hypertension. However, interval of pregnancy after KT was controversial. The aim of this study is to define the relation between graft survival and interval after kidney transplantation.
Patients and Methods: A total 990 recipients of childbearing age underwent KT between April 1979 and December 2014 in our center was enrolled. We retrospectively analyzed the patients dividing into two groups according to interval between KT and pregnancy.
Results: There were 85 pregnancies in 59 women. Among 85 pregnancies, 38 cases showed unsuccessful delivery outcomes such as miscarriage, stillbirth and ectopic pregnancy. Mean age of transplantation were 26.3 ± 4.4 years and age of pregnancy were 31.6 ± 3.9 months. The mean interval from transplantation and pregnancy were 57.5 ± 43.5 months. We divided the 47 deliveries into two group: transplantation to conception interval of less than 2 years in 11 deliveries, and the others in 36 deliveries. Mean serum creatinine was reported before and after pregnancy and no significant changes in its mean value. In the < 2 years group, mean age of delivery was 30.5 ± 4.2 years and incidences of preterm delivery, low birth weight were 18.2%, 45.4% respectively. The patient characteristics were similar between < 2 years group and ≥ 2yeasrs, but age of transplantation was high in < 2 years group (28.6 ± 4.2 vs. 25.5 ± 3.6, $p < 0.05$). The 10 year graft survival rates were also similar between two groups (100% vs. 90%, $p = 0.586$)
Conclusion: There were no significant difference of graft survival in mean interval between transplantation and conception of ≥2 years and < 2 years.

Table 1. Comparison of time interval between kidney transplantation and pregnancy

	<2 years	≥2 years	p-value
Number of deliveries	11	36	
Age of transplantation (years)	28.6 ± 4.2	25.5 ± 3.6	0.022
Age of delivery (years)	30.5 ± 4.2	31.9 ± 3.4	NS
Gestational period (weeks)	37.5 ± 2.1	36.0 ± 2.7	0.035
Preterm delivery (<37 weeks)	2 (18.2%)	22 (61.1%)	NS
Delivery type			
Vaginal delivery	2 (18.2%)	7 (19.4%)	NS
Cesarean section	9 (81.8%)	29 (80.6%)	NS
Birth weight (g)	2604 ± 480	2203 ± 584	0.044
Low birth weight (<2.5 g)	5 (45.5%)	23 (63.9%)	NS

Figure 1. Graft survival rate according to the interval between transplantation and pregnancy



BO338 MACHINE LEARNING METHODS TO PREDICT DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: As delayed graft function (DGF) after kidney transplantation is associated with deleterious short-term and long-term consequences, we want to evaluate the value of novel machine learning methods in the prediction of DGF.
Methods: 497 kidney transplantations from deceased donors at our center between 2005–2011 are included. A feature elimination procedure, based on logistic regression models, is applied to iteratively select a subset of the 7 most influential parameters out of 47 retrospectively collected parameters. Subsequently, 7 distinct machine learning methods are fitted using the reduced data set: logistic regression (LR), linear discriminant analysis (LDA), support vector machines (SVM; using linear and radial basis kernel functions), random forest (RF), decision tree-based model (TBM) and stochastic gradient boosting (SGB). Performance of the models is assessed by computing sensitivity, specificity and area under the receiver operating characteristic (AUROC) after 20-fold cross validation.
Results: The observed incidence of DGF is 12.5%. As SGB, TBM and RF are mainly sensitive and specific in identifying recipients without DGF due to imbalanced data, their discriminative capacity is weak. AUROCs are 67%, 50% and 73% respectively. LDA, and especially linear SVM, radial SVM and LR are significantly more sensitive in identifying recipients with DGF at the expense of specificity, while maintaining an acceptable sensitivity and excellent specificity in identifying recipients without DGF. AUROCs are 79%, 78%, 79% and 79% respectively.

		Sensitivity (%)			Specificity (%)		AUROC (%)
Statistical method	No DGF	DGF	Overall	No DGF	DGF	Overall	(training set / cross validation set)
SGB	100	5	88	88	60	85	91/67
TBM	98	13	87	89	44	83	83/50
RF	100	3	88	88	100	89	87/73
LDA	95	29	87	90	46	85	80/79
Linear SVM	75	68	74	94	28	86	81/78
Radial SVM	84	53	80	93	33	85	80/79
LR	74	71	74	95	28	86	81/79

Conclusion: 7 distinct types of predictive models for DGF are considered. SGB, TBM and RF have a weak discriminative capacity, as they are mainly sensitive in identifying recipients without DGF. LDA, and especially SVMs and LR are sensitive in identifying recipients with and without DGF, resulting in a strong discriminative capacity. Our study demonstrates that LDA, SVMs and LR are most appropriate in predicting DGF.

BO339 RECURRENT LUPUS NEPHRITIS AFTER TRANSPLANTATION: CLINICOPATHOLOGICAL EVALUATION WITH PROTOCOL BIOPSIES

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Objectives: Lupus nephritis (LN) is an important complication of systemic lupus erythematosus (SLE) and cause of end-stage renal disease (ESRD) in 10–25% of the patients. Aim of the study is to determine the clinicopathological findings and outcome of the patients with LN undergoing kidney transplantation (KTx) in the guidance of indication and protocol biopsies. Methods
The patients who underwent KTx due to LN between January 2000 and 2012 were retrospectively analyzed. All the patients met the ACR criteria for SLE. Recurrent LN (RLN) was diagnosed by transplant kidney biopsy.
Results: Among 955 KTx patients, 12 patients with LN as the cause of ESRD were enrolled. Five patients were male. The dialysis duration was 39 ± 46 months. The duration between the diagnosis of LN and KTx was 11 ± 6 years. The mean age at the time of KTx was 35 ± 11 years. Eleven out of 12 patients received prednisolone, MMF/azathioprine and a calcineurin inhibitor as maintenance immunosuppressive therapy. The mean follow-up time was 63 ± 34 months. Mean levels of serum creatinine and proteinuria were 1.55 ± 0.78 mg/dL and 0.26 ± 0.26 gm/day, respectively, in the last follow-up visit. Eighteen indication and 22 protocol biopsies were performed in

all patients and 27 biopsies were also evaluated by immunofluorescence microscopy. Two patients were diagnosed subclinical RLN by protocol biopsies. Clinical recurrence occurred in 4 recipients. Time period from diagnosis of LN to KTx was significantly shorter and use of ATG as induction treatment was significantly lower among patients with RLN. Graft loss occurred only in two recipients who had clinical RLN after 50 and 111 months following KTx. The 5-year overall graft survival was 85.7%. Conclusion

In our study, half of the patients had RLN and only 2 of them had graft loss in a considerably late period. KTx is a reasonable option for patients with ESRD secondary to SLE; however the recurrence of LN is not rare.

BO340 DETERMINANTS FOR KIDNEY ALLOGRAFT FAILURE AND CHRONIC DISFUNCTION

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Despite significant improvements in short-term kidney allograft survival, the rate of long-term chronic graft loss remains substantial. The exact mechanisms responsible for the pathogenesis of chronic disfunction leading to allograft loss are unknown, nevertheless a number of factors have been shown to influence allograft failure. The aim of this study was to analyse retrospectively patients who lost kidney allograft earlier by chronic disfunction versus those with longer kidney survival and compare variables between both groups. We used database from 307 patients with chronic disfunction, who were submitted to kidney transplantation from August 1983 to July 2010. Mean receptor's age at time of transplantation was 33.2 years and 57% were male. The mean and median of kidney allograft survival was 8.9 and 7.7 years, respectively. We divided the sample in two groups, by the median value (8 years) of years of transplant [group 1 (<8 years)=157 and group 2 (>8 years)=150]. Receptor's age were similar in both groups (33.8 and 32.7 years in groups 1 and 2, respectively) ($p = 0.653$), whereas donor's age was superior in group 1 comparatively with group 2 (38.8 vs. 30.4 years) ($p = 0.051$). There was no relation between etiology of chronic kidney disease and early kidney allograft failure, except in the systemic diseases [group 1 = 7.6% ($n = 12$) and group 2 = 2% ($n = 3$)] ($p = 0.019$). Episodes of clinical acute allograft rejection in first year of transplant were more frequent in group 1 (56.1%) than group 2 (40.9%) ($p = 0.006$). Despite degree of sensitization (PRA) was similar in both groups, the four cases of HLA antibodies were observed only in patients of group 1. Donor's age, presence of systemic disease and episodes of acute rejection in first year, were the main determinants for early kidney allograft failure. This is important in screening of candidates to kidney transplantation and prevention of chronic allograft disfunction.

BO341* EVALUATION OF VASCULAR STRUCTURES OF LIVING DONOR KIDNEYS BY MULTISLICE COMPUTED TOMOGRAPHY ANGIOGRAPHY BEFORE TRANSPLANT SURGERY

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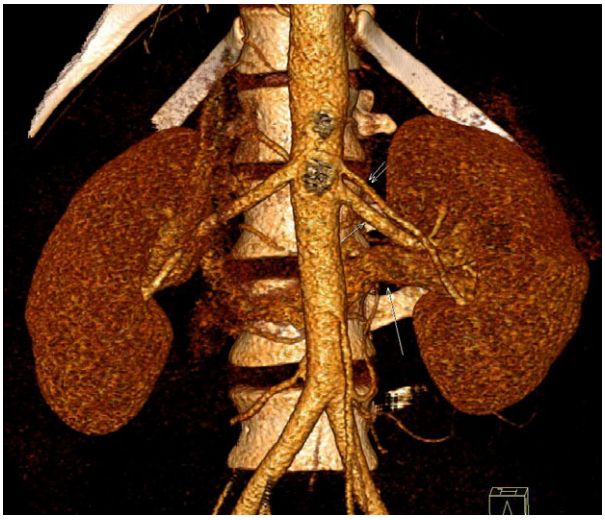
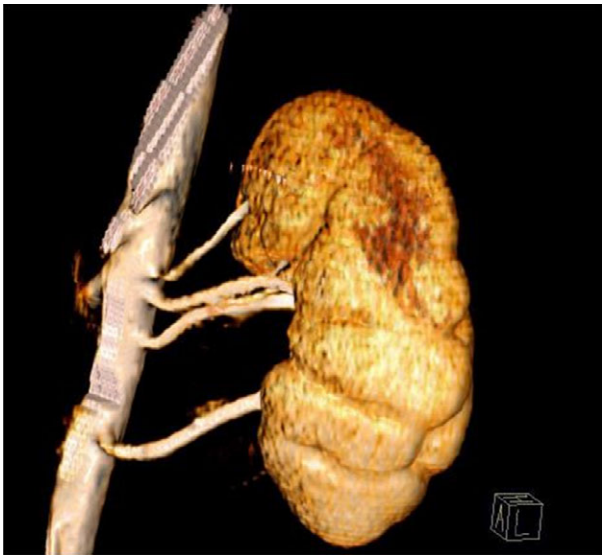
Purpose: Computed Tomography Angiography (CTA) has become the first choice for evaluation of donorkidney vessels. However, many institutions perform multiphasic renal CTA to assess arteries and veins, and thuspatients expose to high amount of radiation. The aim of our study is to determine the efficacy of preoperativearterial CTA in donor nefrectomy, to assess the renal vascular variations of donor kidneys.
Method: Seventy living donor candidates were included to this retrospective study, who had CTA for theassessment of their renal vessels in our hospital between 2011 and 2014. Only arterial phase images wereobtained to avoid exposing the patients from high dose of radiation. Scans were reported by two radiologistsindependently. The number of renal arteries, veins and their tributaries were documented. The donor kidneyswere removed by two consultant surgeons, and after back-table perfusion the same details were recorded andtaken as the reference findings for the operation side. SPSS 13.0 software programme was used for statisticalanalysis, $p < 0.05$ was considered as significant.
Results: A total of 70 potential live kidney donors underwent renal CTA, among them fifty five patients haddonor nefrectomy. A total of 140 kidneys were evaluated by CTA and the vessels of 55 harvested kidneys werecompared with CTA findings. There were 40 kidneys that had at least one accessory or polar artery. There were5 early branching renal arteries, one retroaortic and one circumaortic renal vein. Three kidneys had multiplerenal veins. Interobserver agreement was excellent. Both radiologists found the same results except two cases. Operation findings were totally consistent with CTA findings in patients who underwent donor nefrectomy.
Conclusion: Arterial phase CTA is sufficient for evaluation of both arterial and venous vessels of kidneys, and precontrast, venous or late phase imaging should be preserved only for chosen circumstances to avoid highradiation exposure.





BO342* SEVOFLURANE BASED ANESTHESIA IN RECIPIENTS REDUCES 2 YEAR ACUTE REJECTION IN LIVING DONOR KIDNEY TRANSPLANTATION. RESULTS FROM THE VAPOR-1- TRIAL

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University Medical Center Groningen

Introduction: Volatile anesthetic agents like sevoflurane may protect against the ischemia and reperfusion injury (IRI) and may modify immune cell functions This could have great potential for organ transplantation. Our group set out to optimize the anesthetic regimen in renal transplant recipients. We therefore conducted the VAPOR (Volatile Anesthetic Protection of Renal Transplants) trial. We evaluated the influence of two common anaesthetic regimens, a propofol based versus a sevoflurane based anesthesia, on transplant outcome in living donor kidney transplantation (LDKT). We considered LDKT as the ideal first step as it is a standardized, controlled, procedure with reproducible cold and warm ischemic periods and the absence of profound systemic changes found in postmortal donors.
Methods: In a prospective randomized controlled clinical trial 60 couples were assigned to three groups: PROP; donor and recipient received propofol, SEVO;

both received sevoflurane and SERE; donor received propofol and recipient sevoflurane (n = 20/group). Only left kidney were included because of the gonadal vein as a side branch through which blood samples during reperfusion could be taken. Blood and urine samples were taken at different time points. Renal biopsies were taken during cold ischemia and 1 h after reperfusion. Well definded clinical data of all patients were available.
Results: There were no significant differences between groups in donor and recipient demographics. Acute rejection after two years: PROP 6/17 (35.3%), SEVO 2/19 (10.5%) and SERE 1/20 (5.0%). There was a significant reduction in acute rejection in SERE versus PROP (Fisher exact, p = 0.033) and when SERE and SEVO groups were combined (sevoflurane versus propofol for recipients, as will be studied in VAPOR-2) the difference in acute rejection was even stronger (Fisher exact, p = 0.017)
Conclusion: A sevoflurane based anesthesia significantly reduces acute rejection within 2 years following living donor kidney transplantation

BO343 EXPANDING THE DONOR POOL: RESULTS OF A UK-WIDE NATIONAL SURVEY OF RENAL TRANSPLANT SURGEONS AND OUTCOMES OF A SINGLE CENTRE CASE SERIES OF DUAL KIDNEY TRANSPLANT (DKT)

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Background: Dual kidney transplantation (DKT) involves transplanting both kidneys from a single deceased donor into one recipient, where the kidneys are deemed "unfavourable" for single kidney transplantation (SKT). DKT has increased in popularity over the last decade, although understanding of donor/recipient criteria remains limited.
Methods: (1) An online survey was distributed to consultant renal transplant surgeons in all UK transplant centres. Opinions were sought on donor and recipient criteria regarding suitability for DKT from both DCD and DBD donors. 2) Retrospective outcome data was collected on all DKT performed at our centre from April 2013 to November 2014.
Results: *Survey:* (1)There were 51 Survey respondents; 89% worked at centres that perform DKT. The salient points are summarised in the table below:

Case Series: (2) In our centre, we performed 13 DKT transplants. The Mean donor age was 71 years (range 63–79), of which 23% had diabetes. 77% were DCD donors, 62% had known hypertension and 20% had complex anatomy. Mean recipient age was 65 years (range 49–75). The mean serum creatinine at 1.3 and 6 months was 198, 148, and 128 μmol/L. The average eGFR at 12 months post-op was 70 (+/- 23.1).

Delayed graft function occured in 38%. One recipient developed a lymphocele. Two recipients had a single kidney explanted: One due to renal vein thrombosis, and the other recipient developed a renal artery pseudoaneurysm secondary to vancomycin-resistant enterocccus infection. There was no primary non-function, and no postoperative deaths. The average length of stay was 7.2 days.
Conclusion: (1) There are no internationally-agreed criteria for DKT. This survey has demonstrated that there is a wide variation in national consensus as to acceptable donor and recipient criteria. Whilst some surgeons may accept "extreme" variables, many retain a more conservative approach. 2) Outcomes from our single-centre case series demonstrates that DKT is feasible and successful.

BO344* THE CLINICAL BENEFIT OF PROTOCOL BIOPSIES FOLLOWING KIDNEY TRANSPLANTAION: A SYSTEMATIC REVIEW

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Background: Protocol (or surveillance) biopsies are defined as those taken without specific clinical indication with intention of detecting subclinical changes within the graft. There has been longstanding debate regarding the role of protocol biopsies in renal transplant recipients as biopsy is an invasive procedure with definable risks to graft and recipient, and therefore must be justified by yielding useful information that will modify patient management and improve clinical outcomes.
Methods: A literature search was performed using Medline, Embase, the Transplant Library and the Cochrane library to identify randomised controlled trials (RCTs) that compare use of protocol biopsies (with appropriate clinical response) to biopsies for clinical indication only. Studies were assessed for methodological quality using the Jadad scoring system.
Results: 11 publications from 6 RCTs met inclusion criteria. All of these studies were of low methodological quality with Jadad scores of 2/5. Heterogeneity in baseline immunosuppression, timing of biopsies and length of follow-up precluded meta-analysis and made interpretation difficult. There were some important observations. The benefit of early biopsies to detect subclinical rejection in an era of modern immunosuppression (TAC and MMF) is limited and most benefit is likely to be seen with later biopsies to detect early chronic changes as interstitial fibrosis and tubular atrophy (IF/TA) or CNI toxicity. Existing studies suggest that to assess the benefit of a protocol biopsy program, long-term follow-up of >2 yrs is needed. All studies reported low complication rates from protocol biopsies with no graft losses, suggesting that the practice is safe in experienced hands.
Conclusion: Existing studies are of poor quality and provide conflicting results. However, the lessons from these studies are important and should be used to inform the design of future RCTs to answer this relevant and longstanding question.

BO345* NEGATIVE IMPACT OF ANTI CARDIOLIPID ANTIBODIES ON 1-YEAR RENAL ALLOGRAFT ESTIMATED GLOMERULAR FILTRATION RATE: A COHORT STUDY

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In kidney transplant recipients, antiphospholipid positive tests without antiphospholipid syndrome (APS) were described up to 38% of patients and seem to be associated with thrombotic events. Kidney transplant outcomes and antiphospholipids have not been well described. We conducted an observational, monocentric, retrospective study including 446 renal transplant recipients without APS, SLE or primary coagulation abnormalities. Positivity anticardiolipin (ACL) threshold was 10 UI GPL (ELISA). Patients were screened before

Donor Criteria Variable	Responders Who Would Consider this Acceptable	Recipient Criteria Variable:	Responders Who Would Consider This Acceptable:
Age <55 years	49%	Age <55 years	44%
Age >80 years	51%	Age >75 years	47%
Anti-hypertensives: 3 or more	49%	BMI <20	55%
Type 1 diabetes: >10 years	46%	BMI >40	3%
eGFR <40	24%	Left ventricular ejection fraction <30%	6%
Proteinuria + (30 mg/dl)	70%	Previous PCI >2 Vessels	47%
Proteinuria +++ (>500 mg/dL)	6%	PKD as cause of ESRD	70%
AKI	65%	Pre-dialysis patient	28%
Requiring Haemofiltration	58%	< 1 year dialysis dependent	69%
Haemofiltration >48 h	24%	Any age, NO dialysis options	76%
No pre-transplant biopsy	43%	Inducible ischaemia on dobutamine stress echo	9%
Karpinsky score >6	23%		

transplantation. ACL+ group was defined by at least one positive ACL detection. ACL were screened in 247 patients. Patients screened and not were similar. Among screened patients, ACL- group included 101 patients (59%) and ACL+ group 146 (41%). Mean follow-up was 33.5 (16.6–36) months. Allografts and patients survival were similar between both groups (graft losses: ACL+ $N = 15$ (10%) vs. ACL- $N = 10$ (10%); HR = 1.18). Thrombotic events did not differ between both groups (ACL+ $N = 20$ (20%) vs. ACL- $N = 30$ (21%); HR = 0.98). One year after transplant, eGFR was significantly lower in ACL+ group (48.5 (35.1–60.3) ml/min/1.73 m^2 vs. 51.9 (39.1–65.0) ml/min/1.73 m^2, $p = 0.042$). ACL was an independent risk factor of worst eGFR ($p = 0.03$). ACL without APS before kidney transplantation is an independent risk factor of eGFR decline within the first year post-transplant. Allografts, patients survival and thrombotic events were similar in both groups. Histological analysis of protocol biopsies is in progress.

BO346* 18FDG-PET/CT IMAGING IN SUSPECTED ACUTE RENAL ALLOGRAFT REJECTION

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University of Liege Hospital (ULg CHU)

The diagnosis procedure for kidney transplant recipients (KTR) with suspected acute rejection (AR) relies on needle biopsy. Noninvasive tests to predict nonrejection would be preferable. AR is associated with a recruitment of activated leukocytes into the transplant, which are characterized by a high metabolic activity and an increased uptake of glucose analog, ^{18}Fluoro-deoxy-glucose (^{18}FDG). Thus, ^{18}FDG-Positron emission tomography coupled with computed tomography (PET/CT) may help noninvasively distinguish nonrejection from AR. From January 2013 to February 2015, we prospectively performed 32 ^{18}FDG-PET/CT in 31 adult KTR with suspected renal AR who underwent a biopsy. Biopsies were categorized as "normal", "borderline", "AR" or "others" according to Banff classification. PET/CT imaging was performed within 201 ± 18 min after i.v. administration of 3.2 ± 0.2 MBq/kg of ^{18}FDG, before any modification of immunosuppression. The mean standard uptake values (SUV) of both upper and lower renal poles were measured, with no threshold activity. Biopsies were diagnosed as "normal", "borderline", "AR" or "others" in 8, 10, 8 and 6 (including 3 polyoma-BK nephropathies) cases. Mean SUV respectively reached 1.5 ± 0.2, 1.6 ± 0.3, 2.9 ± 0.8, 2.2 ± 1.2 in each category. Mean SUV of biopsy-proven AR was significantly higher than "normal" cases ($p < 0.01$). No difference was found between "normal" versus "borderline", or between "AR" versus "others" histopathology. Still, a positive correlation between mean SUV and acute composite (g+i+t+v+ptc) Banff score was found, with a coefficient of 0.70 ($p < 0.001$). Sensitivity and specificity of ^{18}FDG-PET/CT in detecting pathological biospies were respectively 92.3% and 36.8%, with a mean SUV threshold at 1.4. ^{18}FDG-PET/CT imaging may help discriminate nonrejection, thereby avoiding unnecessary transplant biopsy in KTR with suspected AR.

BO347* REDUCED INCIDENCE OF CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS RECEIVING EVEROLIMUS

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Background: CMV infection is associated with inferior long-term kidney transplant outcomes. This study compared the incidence of CMV infection/disease in de novo kidney transplant recipients receiving three immunosuppressive regimens and no CMV pharmacological prophylaxis.
Methods: We randomized and treated (1:1:1) 288 low/moderate kidney transplant recipients to receive a single 3 mg/kg dose of rabbit antithymocyte globulin, tacrolimus, everolimus and prednisone (r-ATG/EVR, $n = 85$), basiliximab, tacrolimus, everolimus and prednisone (BAS/EVR, $n = 102$) or basiliximab, tacrolimus, mycophenolate and prednisone (BAS/MPS, $n = 101$). The primary end-point was the cumulative incidence of first CMV infection/disease in the intention to treat population. Secondary end-points included biopsy confirmed acute rejection, graft loss, death, renal function and safety.
Results: Patients receiving EVR showed lower incidence of CMV infection/disease compared to those receiving MPS (4.7 vs. 10.8 vs. 37.6%, $p < 0.001$). There were no differences in the incidence of first treated biopsy confirmed acute rejection (9.4 vs. 18.6 vs. 15.8%, $p = 0.403$), patient (96.5 vs. 95.1 vs. 96%, $p = 0.893$) and graft (95.3 vs. 93.1 vs. 89.1%, $p = 0.267$) survivals. There were no differences in the incidence of wound-healing complications (23.5 vs. 34.3 vs. 22.8%, $p = 0.123$) and delayed graft function (47 vs. 48.5 vs. 41.5%, $p = 0.701$). Mean estimated glomerular filtration rate was lower in BAS/EVR (65.7 ± 21.8 vs. 60.6 ± 20.9 vs. 69.5 ± 21.5 ml/min, $p = 0.021$) respectively, but no differences in proteinuria was observed.
Conclusion: In de novo kidney transplant recipients receiving TAC-based immunosuppressive regimen and no pharmacological CMV prophylaxis, the use of everolimus was associated with a significant reduction in the incidence of CMV infection/disease compared to mycophenolate.

BO348* ECULIZUMAB FOR DE NOVO HUS AFTER KIDNEY TRANSPLANTATION

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Istanbul Memorial Hospital Department of Solid Organ Transplantation

Eculizumab has been used in post-kidney transplant as a rescue therapy in patients with de novo HUS and severe AMR which are resistant to conventional treatments. Between 2012 and 2014, 477 patients underwent living-related kidney transplantation at our institution. All patients received Tacrolimus, MMF and steroid based immunosupression. Among 477 patients, 13 (2.7%) developed de novo HUS, 5 of them (1.04%) needed Eculizumab treatment in which conventional therapies had failed. All the patients who developed de novo HUS post-transplant had no prior history of aHUS and their primary renal disease were different. The diagnosis of de novo HUS was made with elevated LDH, low platelet count, anemia, low haptoglobulin level and schistocytes in peripheral smear. A renal biopsy was done if serum creatine level was elevated. When the diagnosis of de novo HUS was made Tacrolimus was switched to an mTOR inhibitor and plasmapheresis (PP) was initiated. Factor mutations were also evelauated the time of diagnosis Eculizumab was given if patients were resistant to conventional treatment. All renal biopsy results show thrombotic microangiopathy (TMA) compatible with denovo HUS. In one patient who had severe de novo HUS on postoperative day (POD) 2 with oligouria and rising creatinine, a graft biopsy on POD 4 showed diffuse TMA rapidly progressing to cortical necrosis. Eculizumab was started on POD 7 without waiting the clinical response for conventional therapies to save the graft.

Eculizumab is a viable treatment option in patients with de novo HUS post-transplant when the conventional treatment modalities fail. Given the bad prognosis for renal transplantations displaying acute injury progressing rapidly to cortical necrosis on the biopsy, the prompt use of eculizumab could have the advantage of immediate effects by stopping cellular injury. This can provide a therapeutic window to allow conventional treatment modalities to be effective and prevent early graft loss.

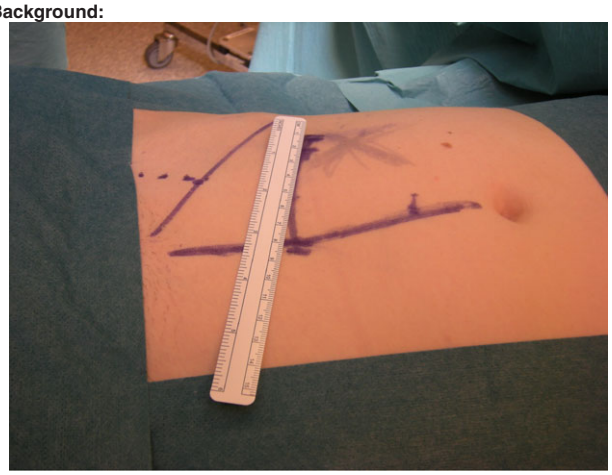
	Age	Female/ Male	Primary Kidney Dis	Duration of Dialysis	Donor	HLA match	Timing of HUS diagnosis	Timing of Inc Creat	Timing of BX	Pathology	PP	Eculizumab treat started	Last Creat	Genetic Mutations
1	26	F	HT	3 year	Father	1 Haplotype	POD 4	POD 3	POD 11	TMA	POD 26	POD 22	1,8	Factor H+, Factor I +
2	4,5	M	BARTTER	4 year	Grandmother	-	POD 2	POD 9	POD 18	TMA	POD 10	POD 11	1,45	N/A
3	30	F	VUR	3 year	Mother	1 Haplotype	POD 3	POD 2	POD 4	TMA+Cort Necr	POD 13	POD 7	1,95	Factor H+, Factor I +
4	31	M	TAKAYASU ARTERİTİS	1 year	Brother	Identical	POD 4	POD 3	POD 4	TMA	POD 28	POD 48	1,56	Factor H+, Factor I +
5	44	F	HT	4 month	Father	1 Haplotype	POD 14	POD 10	POD 13	TMA	POD 41	POD 72	3,2	FactoR H -, Factor I -

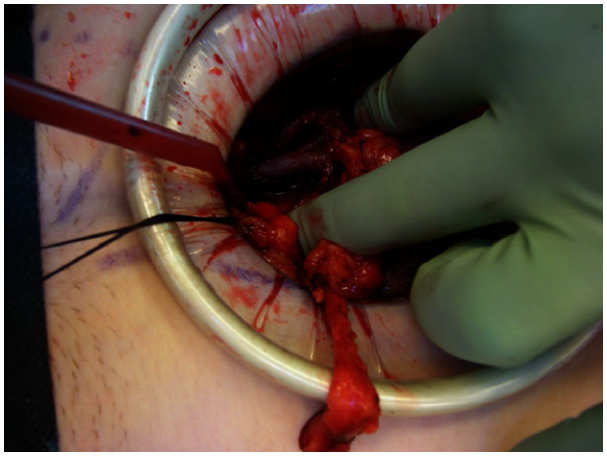
BO349

MINIMAL INVASIVE KIDNEY TRANSPLANTATION IN SIMULTANEOUS LIVER AND KIDNEY TRANSPLANTATION

Niclas Kvarnström, John Söfteland, Annette Lennerling, Michael Olausson
Sahlgrenska University Hospital

Background:





Simultaneous liver-kidney transplantation (SLK) will induce a major surgical trauma. Introducing minimal invasive kidney transplantation can diminish the trauma. It may further influence the results in organ function, surgical complications and physical recovery. We now report our first series of SLK with a minimal invasive technique developed at our centre.

Material and Methods: Three cases were performed with single artery kidney grafts from the same donor as the liver grafts. The liver transplantation with a L-shaped incision was first completed. An atraumatic circular retractor (Alexis®) was placed in a 8 cm transverse incision 5 cm above the inguinal ligament. After creation of a pre-peritoneal cavity for the transplant, the external iliac vessels and bladder were minimally dissected. Before placing the kidney into the wound, the cavity was pre-cooled with ice slush. A semi-automated non penetrating closure system for vascular anastomoses (AnastoClip®) was used for both the venous and artery anastomoses. The ureter was implanted in the top of the bladder using conventional technique.

Results: There were no instances of delayed graft function or surgical complications. Hospital stay ranged from 8–10 days. Operating time (skin-to-skin) ranged from 80–90 min. In case two, there was a proximal ureter stenosis that developed three months after the surgery. It was treated with a double pigtail catheter. Measured GFR (iohexal clearance January 2015) at one-year follow up was 62 for the first patient. He was on dialysis before the transplantation.

Conclusion: Our first series of minimally invasive kidney transplantation in SLK demonstrated excellent patient outcome. Despite being a small pilot series the results look promising for the development of minimally invasive kidney transplantation.

Recipient age, years	Gender, male = M, female = F	OR time, skin to skin, minutes	Kidney start, day*	Hospital stay, days	Lenght of follow up, months

1. *Continued*

Recipient age, years	Gender, male = M, female = F	OR time, skin to skin, minutes	Kidney start, day*	Hospital stay, days	Lenght of follow up, months
66	M	88	1	10	13
53	M	90	1	9	5
57	M	80	1	8	2

BO350*

IMPACTS OF URETERIC STENT REMOVAL TIMING ON POST RENAL TRANSPLANT MAJOR UROLOGICAL COMPLICATION. A SINGLE CENTRE EXPERIENCE

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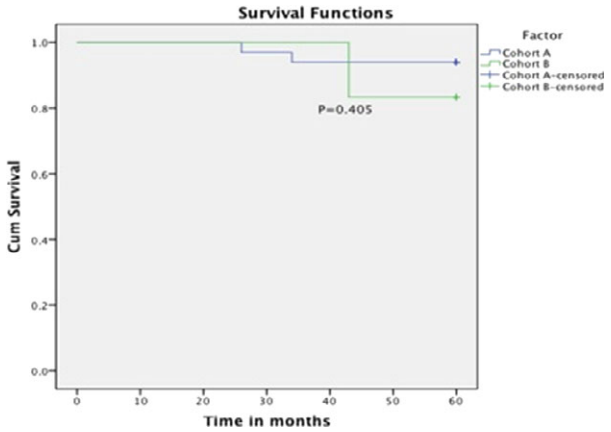
Background: Renal transplant (RTx) has high allograft success rate but is also associated with some potential complications. Urinary leak, ureteric stenosis and stricture are few such major urological complications (MUC) that can result from transplant ureteroneocystostomy. To prevent such complications different techniques of ureteroneocystostomy are used some with Double J ureterovesical stents (JJ-stent) and some without. The timing of postoperative removal of these stents varies considerably between 7 days to six weeks. In King Faisal Specialist Hospital (KFSH) this is a common practice to remove urinary catheter with JJ-stents on 4th postoperative day. In this present study we describe our experience with JJ-stent removal on 4th post opt day following Adult RTx. Material and

Methods: In this retrospective study we analysed outcome of patients for MUC between Jan 2004 and Dec 2013. In our renal database all the information are prospectively logged including all the demographics, outcome and complications. We divided the patient into two cohorts; cohort A where JJ-stent was removed in 4 days and cohort B where the stent was left longer then 4 days. We compared risk incidence of MUC between the two cohorts. We used SPSS 21 for statistical analysis and a p value of <0.05 was considered statistically significant.

Results: A total of 39 (3.06%) MUC including 8 ureteric leaks and 31 ureteric stenosis were recorded among 1271 Adult RTx. Majority of patients had their stents removed within 4 postoperative days (cohort A $n = 1052$) compared with more then 4 days (Cohort B $n = 219$). There was no significant MUC risk recorded between two cohorts [RR 1.1406; 95% CL 0.8591 to 1.8966; $p = 0.7638$]. General demographics and complications are in Table 1. There was no significant survival or hazard function difference between the two groups [$p = 0.405$].

Demographic	Cohort A ($n = 39$)	Cohort B ($n = 6$)	Significance
Donor gender ratio male: female	3:1	5:1	
Recipient gender ratio male: female	3:1	1:1	
Donor age (Median and range)	33 (R: 27–66)	30.5 (R: 21–37)	0.6422
Recipient age (Median and range)	41 (R: 19–77)	40.5 (R: 18–63)	0.7824
Live donor	28	5	0.7492
Deceased donor	11	1	0.4265
Single renal artery	31	5	0.6822
Multiple renal arteries	8	1	0.6944
Recipient BMI (Median and range)	28.5 (R: 17–33)	28 (R: 19–31)	0.8242
CIT in minutes (Median and range)	209 (R: 53–1440)	155.5 (R: 67–1332)	0.0028
Ureteric leak	8	1	0.6298
Ureteric Stricture	31	5	0.5920



Conclusion: Removal of JJ-stent at 4th postoperative day is a safe option with not increased risk of MUC.

025 LIVER

BO351 EARLY OUTCOMES OF LIVER TRANSPLANTS IN PATIENTS RECEIVING ORGANS FROM HYPERNATREMIC DONORS

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Background: Uncorrected hypernatremia in organ donors has been associated with poor graft or patient survival during liver transplants. However, recent studies have found no association between the donor serum sodium and transplant outcome. This study sought to show the negative effect donor hypernatremia has on initial liver allograft function. This is the first study to investigate international normalized ratio and renal factors of patients with normal and those with hypernatremic donor livers.
Methods/Materials: This study was conducted at the Shiraz Transplant Research Center in Shiraz, Iran, between May 2009, and July 2011. Four hundred seven consecutive adult orthotopic liver transplants were performed at the University of Shiraz Medical Center.
Results: There were 93 donors in the group with hypernatremia with terminal serum sodium of 155 mEq/L or greater (group 1), and 314 with terminal serum sodium less than 155 mEq/L (group 2). Posttransplant data after 5 days showed that aspartate aminotransferase, alanine aminotransferase, international normalized ratio, and kidney function did not differ between the groups.
Conclusions: Hypernatremia is the most important complication after brain death. Previous studies have suggested donor hypernatremia results in a greater incidence of early postoperative graft dysfunction in liver transplant and is considered one of the extended criteria donor. However, in recent years, this hypothesis has been questioned. Our study shows no difference between patients' initial results of liver and kidney functioning with normal and hypernatremic donor livers. This is the first study to investigate international normalized ratio as a fundamental factor in defining early allograft dysfunction and renal factors between patients with normal and hypernatremic donor's livers.

BO352 POSTTRANSPLANT PEAK C-REACTIVE PROTEIN IS AN INDEPENDENT PREDICTOR OF RECURRENCE-FREE OUTCOME IN LIVER TRANSPLANT PATIENTS WITH HCC

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Background: Surgical stress by ischemia reperfusion (I/R) injury creates a systemic "pro-inflammatory" environment that may promote tumor outgrowth in liver transplant patients with hepatocellular carcinoma (HCC). C-reactive protein (CRP) is a parameter of inflammatory response. The aim of this trial was to determine the prognostic value of early posttransplant peak CRP-level following liver transplantation (LT) for HCC.
Material/Methods: A total of 103 liver transplant patients with HCC were included. Based on explant histopathology data, patients were classified as Milan In and Milan Out. ROC-analysis has defined an optimal cut-off peak CRP-level of 3.5 mg/dl for overall and recurrence-free survival. The impact of low (≤ 3 mg/dl; $n = 38$) and high (> 3.5 mg/dl; $n = 65$) CRP values along with other established clinicopathologic variables were assessed by uni- and multivariate analysis.
Results: The overall 1- and 5-year survival rates post-LT were 96.9% and 85.7% in the low CRP-group, but 89.7% and 58.5% in the high CRP-population ($p = 0.002$). Five patients in the low CRP-group (7.8%), but 19 patients of the high CRP-subset (48.7%) dveloped HCC relapse post-LT ($p < 0.001$). Microvascular invasion (Hazard ratio [HR] 10.9), high CRP-value (HR 4), AFP-level > 400 IU/ml (HR 3) and total ischemia time > 450 min (HR 3.4) were identified as independent predictors of tumor recurrence. In Milan In patients, CRP level had no prognostic power. In contrast, peak CRP-value (HR 5.8) together with microvascular invasion (HR 8.3) remained as the only independent and significant predictors of recurrence-free outcome. The 1- and 5-year recurrence-free survival rates in this special subset were 94.4% and 88% in the low CRP-group, but only 87.8% and 29.3% in the high CRP-patients ($p < 0.001$).
Conclusion: Early posttransplant peak CRP-levels correlate with risk of tumor recurrence in liver transplant patients with HCC. In particular patients with advanced HCC may possibly benefit from targeting inflammatory mechanisms.

BO353 EARLY PREDICTORS OF LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION IN HCV-NEGATIVE RECIPIENTS

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Introduction: The non-improvement in >1-year post-liver transplant (LT) survival and the diminishing importance of HCV-related issues with modern antivirals call for identification of pre- and early post-LT factors predictive of long-term outcome in HCV-negative recipients.
Methods: This nationwide study included all HCV-negative adult patients transplanted in Finland 1982–2012 with at least 1-year graft survival ($n = 686$, mean follow-up 9.2 years, range 1–29 years). Data were from the Finnish LT registry. We tested 37 pre- and early post-transplant variables for their association with >1-year combined graft loss and mortality, late rejection, cancer, or infections by univariate and multivariate Cox-regression analysis. Impact of immunosuppression regimen was tested on these outcomes and on recurrent autoimmune liver disease and changes in renal function.
Results: Multivariate factors associated with various outcomes >1-year post-LT are shown in the table. Young age predisposed to acute/chronic rejection, and old age to immunosuppression toxicity. Among immunologically stable patients (ALT<50 IU/L and ALP<100 IU/L at 1 year and absence of multiple or severe acute rejection or chronic rejection <1 year) transplanted after year 2000, type of CNI or antimetabolite or steroid use at 1 year had no significant effect on risk for >1-year graft loss/mortality, late rejection, cancer, or infection. Among immunologically unstable patients (at least 1 of above criteria), a benefit of tacrolimus over cyclosporine emerged on graft loss/mortality (HR 0.49, 95% CI 0 –25–0.97, $p = 0.04$). Azathioprine ($p = 0.04$) and steroids ($p = 0.001$) were protective against recurrent PBC. Immunosuppression type had no significant impact on the decline in renal function between years 1 and 10.
Conclusions: Patients with either pre-transplant liver or biliary cancer, poor renal function, early post-transplant infections, or elevated markers of cholestasis represent a risk group that warrants closer long-term follow-up. Patient age emerged as a relevant factor to guide the level of long-term maintenance immunosuppression.

Graft loss or death	Hazards ratio	95% CI	p
Male	2.14	1.45–3.15	<0.001
HCC	2.66	1.45–4.87	0.002
CCC	15.7	5.53–44.3	<0.001
Hypertension	0.44	0.31–0.64	<0.001
GFR at 1 yr	0.99	0.978–0.995	0.002
ALP at 1 yr	1.005	1.003–1.006	<0.001
Bilirubin at 1 yr	1.004	1.000–1.008	0.04
CMV infection <1 yr	1.55	1.06–2.25	0.02
Non-CMV infection <1 yr	1.69	1.16–2.47	0.006
Acute or chronic rejection			
Age	0.98	0.958–0.998	0.03
ALP at 1 yr	1.002	1.000–1.005	0.04
Cancer			
Age	1.03	1.01–1.05	0.001
Male	1.60	1.03–2.47	0.04
Autoimmune hepatitis (chronic)	3.03	1.20–7.65	0.02
Infections			
Age	1.02	1.003–1.03	0.02
LT after 2008	0.47	0.26–0.88	0.02
Hypertension	0.65	0.46–0.91	0.01
Diabetes	1.59	1.12–2.27	0.01
Non-CMV infection <1 yr	1.75	1.25–2.45	0.001

BO354 INFLUENCE OF RECIPIENT GENDER ON LIVER TRANSPLANT OUTCOMES: A SUBGROUP ANALYSIS OF H2304 STUDY

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Purpose: Recipient gender may affect post-transplant (Tx) outcomes. In the H2304 study, treatment with everolimus (EVR)+reduced tacrolimus (rTAC), 4 weeks post-liver (L) Tx, showed comparable efficacy and superior renal function versus standard TAC (TAC-C). Here, we present the influence of gender on efficacy, renal function (estimated glomerular filtration rate [eGFR]) and safety outcomes at M12 post-LTx.
Methods: H2304, a 24-M, multicentre, open-label, controlled study randomised 719 *de novo* LTx recipients (LTxR) (1:1:1) to EVR (C0 3–8 ng/ml)+rTAC (C0 3–5 ng/ml; $N = 245$) or EVR (C0 6–10 ng/ml)+TAC withdrawal

(TAC-WD; $N = 231$) at M4 or TAC-C (C0 6–10 ng/ml; $N = 243$). Primary efficacy endpoint was the composite efficacy failure rate (treated biopsy-proven acute rejection, graft loss or death) at M12. Key secondary endpoint was the evolution of eGFR from randomisation (RND) to M12 by MDRD4.
Results: 73.5% and 73.7% of LTxR were male in EVR+rTAC and TAC-C arms, respectively. At M12, the incidence of composite efficacy failure was lower for both genders in the EVR+rTAC (Table). Irrespective of gender, change in eGFR from RND to M12 was better in the EVR+rTAC versus TAC-C arm (male: −3.65 vs. −8.42 ml/min/1.73 m^2 [p = 0.082] and female: −0.05 vs. −15.17 ml/min/1.73 m^2 [p < 0.001]). Overall, the incidence of adverse events was comparable between gender and treatment arms (EVR+rTAC; male: 95.0%; female: 93.8% vs. TAC-C; male: 96.1%; female: 92.1%). In the EVR+rTAC arm, the incidence of peripheral oedema was higher in female (29.2%) vs. male (13.3%), whereas in the TAC-C arm it was higher in males (11.8%) vs. in female (7.9%) LTxR.
Conclusion: Independent of gender, H2304 study data showed the lower incidence of efficacy failures and better eGFR with EVR+rTAC versus TAC-C at M12. Renal function was significantly better in female recipients compared to males treated with EVR, which needs to be confirmed by further investigations.

Table: Incidence rates of primary composite efficacy failure, tBPAR, graft loss or death

Parameters, n (%)	EVR+reduced TAC (N=245)		TAC control (N=243)	
	Male (n=180)	Female (n=65)	Male (n=179)	Female (n=64)
Primary composite efficacy failure*	13 (7.2)	3 (4.6)	17 (9.5)	6 (9.4)
tBPAR	5 (2.8)	2 (3.1)	12 (6.7)	5 (7.8)
Graft loss or death	10 (5.6)	2 (3.1)	6 (3.4)	1 (1.6)

*Includes tBPAR, graft loss or death.
EVR, everolimus; TAC, tacrolimus; tBPAR, treated biopsy proven acute rejection

BO355 FACTORS AFFECTING GRAFT SURVIVAL AFTER LIVER TRANSPLANTATION WITH THE USE OF AORTOHEPATIC CONDUITS

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Introduction: The use of aortohepatic conduit in orthotopic liver transplantation (OLT) is occasionally required, especially when the native arterial supply is compromised. Aortohepatic conduits are described to confer a higher risk of post-operative complications, especially hepatic arterial thrombosis. Our study investigates the outcomes of the use of aortohepatic conduits in OLT.
Methods: This is a retrospective single centre analysis of prospectively collected data from our institution's electronic database. All patients undergoing OLT with the use of an aortohepatic conduit, between January 2003 and October 2014, were included. Patient and graft outcomes and complications were investigated with descriptive statistics. Patient and graft survival was estimated using the Kaplan-Meier method. Univariate and multivariate statistical analysis was performed to identify potential risk factors affecting survival.
Results: Out of 891 patients who underwent OLT, 86 (9.7%) received 92 liver grafts using aortohepatic conduits. The male to female ratio was 52:34 (60.5%:38.5%) and the median age was 51 years (range: 19–69). Median follow-up was 45 months (range: 0–144). Twenty deaths were recorded during the follow-up period, with patient survival at 12 years being 65.4%. During the follow-up period, 19 grafts failed, including 10 (53%) due to a conduit-related complication.

Graft survival at 12 years was 72.3%. The overall complication rate was 34% (31 cases), with 16.3% (15 cases) being directly related to the conduit (thrombosis, bleeding, stenosis). No difference was identified in graft survival between supra-coeliac and infra-renal conduit placement. Amongst infra-renal conduits, ante-pancreatic placement was associated with worse graft survival compared to retro-pancreatic placement.
Conclusion: The use of aortohepatic conduit is a useful technique in OLT with acceptable long-term patient and graft survival, despite an increased risk of post-operative complications.

BO356* IMPACT OF ABERRANT LEFT HEPATIC ARTERY LIGATION ON OUTCOME AFTER LIVER TRANSPLANTATION

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Introduction: The incidence of left hepatic arteries with aberrant origin (from left gastric artery, aorta, splenic artery, celiac trunk, etc.) in donors is about 35%. The reconstruction of these arteries at liver transplantation (LT) can ensure the proper vascularization of the left liver but can also be a risk factor for hepatic artery thrombosis. We retrospectively analyzed the postoperative impact of the intraoperative ligation of aberrant left hepatic arteries of the graft versus preservation of aberrant left hepatic arteries after LT.
Materials and methods: From 8-2005 to 4-2014 we performed 319 liver transplants. In 87 (27.3%) grafts there were abnormalities of the arterial vascularization. In 51 (16%) grafts there was an aberrant right hepatic artery (49 arising from the superior mesenteric artery, 1 from superior mesenteric artery, 1 from celiac trunk). In 46 (14.4%) grafts there was an accessory left hepatic artery (42 from left hepatic artery, 2 from celiac trunk, 2 from the aorta), in 4 graft the common hepatic artery arises from superior mesenteric artery (hepato-mesenteric trunk).
Results: In 18/46 (39.1%) patients the accessory left hepatic artery was intraoperatively ligated (LHAL Group), while in 28/46 (60.9%) patients the aberrant left hepatic artery was preserved (LHAP Group) using the celiac trunk of the graft or with an anastomosis with the gastroduodenal artery of the graft. 1–3 years graft survival was 89.3–89.3% in LHAL Group vs. 85.6–85.6% in LHAP Group (p = 0.45). After a mean follow-up of 40.7 ± 31.9 months, 1 (5.5%) late hepatic artery thrombosis occurred in LHAL group, while 2 (7.1%) hepatic artery thrombosis (one early and one late) occurred in the LHAP group (p = 1). In LHAL group 3 (16.7%) anastomotic biliary strictures occurred versus 10 (35.7%) in the LHAP group (p = 0.20).
Conclusion: Intraoperative left hepatic artery ligation does not provide an increased risk of hepatic artery thrombisis or biliary complications after LT.

BO357 WAITLIST MORTALITY AND SURVIVAL AFTER LIVER TRANSPLANTATION IN PATIENTS WITH CHOLESTATIC LIVER DISEASE – THE MELD ERA

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Medical University of Vienna

Background: Liver transplantation (LT) for cholestatic liver disease has shown favourable outcome. The impact of MELD introduction (MELDi), however, remains to be elucidated. We analysed waitlist mortality and post transplant patient survival in primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) prior to and after MELDi in Vienna.
Methods: All adult patients (pts) listed for LT for PSC or PBC between 1983 and 2014 were included. After MELDi in 2007, pts with PBC were listed according to labMELD, and PSC pts according to the highest MELD during active cholangitis. In addition, all pts received 1 waiting point per month
Results: In total, 168 pts were analysed, 98 pts with PBC (88% female; median age: 55a, range: 27–69) and 70 pts with PSC (47% female; median age: 46a, range: 20–73). Waitlist mortality in all pts was 11%. Waitlist mortality in PBC until 2007 was 13% and 25% thereafter (p = 0.261), and 3% vs. 9% (p = 0.325) in PSC. Overall 1y – pt survival after LT was 81.2%, 5y-pt survival was 72.2%. Pts listed after MELDi showed an increased 1y- (78.8% vs. 88.2%; p = 0.219) as well as 5y-survival (68.7 vs. 82.4%; p = 0.213) independent of the indication for LT. Regarding PBC and PSC pts separately showed similar 1y-survival (80.8 vs. 81.8%), but superior 5y-survival for PSC (67.9 vs. 78.2%). Both 1y- and 5y-survival improved after MELDi in PBC and PSC by up to 22%. One year after LT 100% of PBC, and 83.3% of PSC pts listed after MELDi were still alive compared to 77.9% (p = 0.114) and 80.6% (p = 0.781) of pts listed before. Five years after LT 80% of PBC pts, and 83.3% of PSC pts were alive compared to 66.2% (p = 0.475) and 74.2% (p = 0.501) listed before MELDi.
Conclusion: PSC pts show superior short- and long-term survival compared to PBC. Overall 1y- and 5y- patient survival increased by up to 22% after MELDi. MELD in combination with waiting points as used in Vienna did not impair outcome after LT for cholestatic liver disease.

BO358 USE OF LIVER GRAFTS ≥80 YEARS: THE LESSONS LEARNED AFTER OVER 150 TRANSPLANTS

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Background: We have previously demonstrated that elderly (≥80 years) grafts may provide favorable long-term results after liver transplantation (LT). However, they are associated with an increased risk for ischemic-type biliary lesions (ITBL) and hepatitis C virus (HCV) recurrence after compared to standard donor grafts.
Methods: This was a retrospective, case-control analysis on use of elderly liver grafts (≥80 years) for LT at a single institution. From January 2003 thru June 2014, 154 LT were performed with deceased donors ≥80 years vs. 131 with donors 18–39 years. Patients were matched on a 1:1 basis as per indication to LT, model for end-stage liver disease (MELD) score at transplantation, cold (CIT) and warm ischemia time (WIT). Finally, a total of 106 recipients of grafts ≥80 years (Group A) were compared against 106 recipients of standard donor grafts (18–39 years, Group B). The primary end-point was graft and patient survival rate between the groups. The secondary end-point was assessment of ITBL and HCV-related graft loss. Graft survival was censored at time of re-listing or re-transplantation. Patient survival was censored at time of death, lost to follow-up or as of December 2014. Survival

rates were according to Kaplan-Meier and the level of statistical significance was set at 5%.
Results: In Group A vs. Group B, HCV-related graft loss was 20/106 (18.9%) vs. 6/106 (5.7%) ($p = 0.0059$; OR = 3.87); incidence of ITBL was 16/106 (15.1%) vs. 6/106 (5.7%) ($p = 0.040$ OR = 2.96), and incidence of ITBL-related graft loss was 5/106 (4.7%) vs. 0 (0%) ($p = 0.059$). ITBL-related patient death was 3/106 (2.8%) vs. 0 (0%) ($p = 0.246$) in Group A and B, respectively. Graft survival was 90.9%, 84.9%, and 75.8% at 1, 3 and 5 years in Group A vs. 92.5%, 88.4%, and 87.2% in Group B ($p = 0.03$, log rank).
Conclusions: Although associated with a 5-year graft survival rate of 75.8%, liver donor grafts ≥80 years have a 4-fold increased odds for HCV-related gra

BO359 LIVER TRANSLANTATION FOR END STAGE LIVER DISEASE CAUSED BY AUTOIMMUNE HEATITIS AND OVERLAP SYNDROM, LONG TERM FOLLOW UP

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Background: Liver transplantation is the treatment of choice for end stage liver disease caused by various etiologies. The three major types of immune disease of liver are primary sclerosing cholangitis (PSC),primary biliary cirrhosis (PBC)and autoimmune hepatitis (AIH). Variant types are called overlap syndrome but there is no consensus for definition and diagnosis of this syndrome.
Methods/materials: In this study we analyzed postoperative complications (acute and chronic rejection, biliary complication, recurrence after liver transplantation)of patients with autoimmune hepatitis and overlap syndrome which underwent liver transplantation in shiraz transplant center between sep.2000 to april 2008. Median follow up was 105 (82–172) months. Patients labeled as overlap syndrome according to paris criteria .
Results: Long term follow up (for 31 cases with AIH and 17 cases with overlap syndrome) revealed that chronic rejection and biliary complications after liver transplant are significantly more common in patients with overlap syndrome.

Etiology	Num. of cases	Episodes of acute rejection	Documented chronic rejection	Biliary complications	Documented recurrence
autoimmune hepatitis	31	17	1	3	1
overlap syn	17	10	3	3	0

Conclusion: Recently number of AIH_PSC cases dramatically increased in our center parallel to number of transplantations. In this study we couldn't use all these data due to short term follow up, but we showed that in overlap cases, postoperative evaluations should be more intensive to achieve acceptable results in this large group of patients.

BO360 LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION FOR HEPATIC SCHISTOSOMIASIS: A SINGLE-CENTER EXPERIENCE OVER 15 YEARS

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Our objective was to study the long-term outcomes of patients who had undergone liver transplantation because of schistosomiasis at our institute over the last 15 years. Four hundred forty-one patients underwent liver transplantation at our institute, and14 did so for schistosomiasis. The survival of patients who underwent transplantation for schistosomiasis was compared with that of patients who underwent transplantation for other liver diseases. Survival curves were drawn via the Kaplan-Meier method and were compared with the log-rank test. $p < 0.05$ was considered significant. All 14 patients were male, and the average age was 56.8 ± 8.4 years. The average Model for End-Stage Liver Disease score was 18.2 ± 5.6, and the average Child-Pugh score was 10.6 ± 1.2. All patients had splenomegaly; pretransplant variceal bleeding occurred in 7 patients (50%), and portal vein thrombosis was diagnosed in 5 patients (36%). Patient survival was 75% 1 year after transplantation and 75% at the end of follow-up because no patients were lost after the first year. Patients who underwent transplantation for other causes achieved survival rates of 86% and 76% 1 and 10 years after transplantation, respectively. There was no significant survival difference between the 2 groups ($p = 0.66$). All patients who survived the early posttransplant period had functioning liver grafts with no reported diagnoses of schistosomiasis in the new grafts. In conclusion, liver transplantation for patients with schistosomiasis has a favorable outcome with no risk of reactivation.

011 HEART

BO361 CMV COMPLICATIONS AFTER HEART TRANSPLANTATION – A SINGLE CENTER ANALYSIS

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Background: Cytomegalovirus (CMV) as a major cause of infectious complication after heart transplantation (HTX) is associated with viral syndrome and gastrointestinal symptoms but also with rejection, development of graftvasculopathy (CAV), graft loss and mortality. At the Medical University of Vienna, a standardized protocol for CMV diagnoses with CMV-PCR and prophylaxis/treatment of CMV with Anti-CMV hyperimmunoglobuline and valganciclovir has been used since 2002. The aim of this analysis was to evaluate the CMV complications that occurred in the last 12 years.
Methods: 348 adult 1-month survivors after HTX (median age 55a, 24% female, transplanted between 2002 and 2012) were scored into 4 groups according to the CMV recipient and donor serostatus (R/D: +/+; +/-; -/-; -/+). High-risk group (-/+) received valganciclovir prophylaxis for three months post HTX. The association between CMV matching and complications as well as between CMV infection and complications including CAV and survival were tested with weighted Cox regression analysis.
Results: CMV infection occurred in 33% (*n* 114) and CMV disease in 7% (*n* 23). 21 patients had a second infection, 4 a third and 2 a fourth. Median time to infection was 1.5 months compared to 6 month in the high-risk group with prophylaxis. The high-risk group (24%) had the highest infection rate ($p < 0.07$; HR 0.69) and CMV associated symptoms ($p < 0.01$; HR: 8.22), the low-risk group (-/-) the lowest rate of infection ($p < 0.0001$, HR: 0.07) and disease ($p < 0.0001$, HR: 0.12). Infection was not associated with a higher risk of CAV ($p = 0.72$; HR 1.01) but with borderline worse survival ($p = 0.08$; HR 1.61).
Conclusion: In our data, CMV associated complications occurred rarely. Infection was not associated with CAV but with worse survival. The high-risk group had higher risk of infection and CMV disease.

BO362 CHANGING TO CT ANGIOGRAPHY FOR THE SURVEILLANCE OF GRAFT VASCULOPATHY AFTER CARDIAC TRANSPLANTATION: A MORE COST EFFECTIVE INVESTIGATION?

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Purpose: To consider the use of CT angiography in the setting of surveillance for cardiac allograft vasculopathy.
Material and Methods: Retrospective review of CT angiograms performed in heart transplant recipients between October 2013 and September 2014. Positive results in this cohort of patients were compared with positive results in a comparator cohort who had surveillance coronary angiography in the previous year. The positive predictive value of CT angiograms was compared with the positive predictive value of coronary angiograms performed between October 2012 and September 2013. Nuclear myocardial perfusion imaging was used as the standard to confirm the presence of ischaemia due to significant disease.
Results: The outcome of 159 CT angiograms was reviewed. New abnormalities were detected in 13 scans: in one patient a severe stenosis diagnosed by CT was investigated further by conventional coronary angiography which failed to identify a significant stenosis and therefore myocardial perfusion imaging was not indicated; of the remaining 12 patients, 7 had positive myocardial perfusion scans; i.e. 7/13 were deemed positive giving a positive predictive value of 53.8%. 155 patients had coronary angiograms in the previous year. Significant abnormalities were detected in 7 patients of whom 3 had positive myocardial perfusion scans giving a positive predictive value of 43%.
Conclusion: This retrospective review of heart transplant patients undergoing surveillance for graft coronary artery disease demonstrated a comparable positive predictive value in CT angiography as compared with coronary angiography. CT angiography has the added benefits of avoiding the risks of an invasive procedure and negated the need of overnight stay saving bed costs and improving patient experience. CT angiography appears to be a superior modality within this clinical context.

BO363 POTENTIAL ROLE OF RECIPIENT'S HEME OXYGENASE-1 PROMOTER REGION POLYMORPHISM IN CARDIAC ALLOGRAFT VASCULOPATHY

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Background: Cardiac allograft vasculopathy (CAV) remains one of the leading causes of death in heart transplant patients. Heme oxygenase-1 (HO-1) catalyzes the rate-limiting step in the degradation of heme to biliverdin, free iron and carbon monoxide. It mediates anti-inflammatory and anti-oxidative effects. The promoter region of HO-1 has been shown to contain a highly polymorphic (GT)*n* repeat, where a higher transcriptional activity is linked to shorter (GT)*n* repeat sequences. Numerous studies have shown the potential protective effects of HO-1 in cardiovascular diseases, but recent trials also revealed a conflicting role in chronic inflammatory diseases.
Methods: Recipient HO-1 (GT)*n* repeat polymorphism was analysed in 344 heart transplant patients, of which 144 were classified as positive for CAV. HO-1 genotype was divided according to the number of GT repeats into "short" (GT <27) and "long" (GT >= 27). A possible relation to CAV was analysed using logistic regression including common risk factors for CAV.
Results: Donor age (OR 1.044 (CI 1.023–1.064); $p < 0.001$), years from transplant to diagnosis (OR 1.049 (CI 1.012–1.087); $p = 0.009$) and previous smoking (OR 4.117 (CI 1.646–10.295); 0.01) were significant predictors for CAV. HO-1 genotype showed a potential effect in this model ($p = 0.078$), whereas the short GT length polymorphism group revealed a higher risk for CAV (OR 2.211 (CI 1.053–4.644); $p = 0.036$).
Conclusion: Recipient HO-1 genotype may have an effect in CAV development. This finding has to be evaluated in larger series including studies targeting the underlying disease mechanism.

BO364 ELEVATED PRETRANSPLANTATION SOLUBLE BAFF: A NEW BIOMARKER FOR ACUTE CELLULAR REJECTION RISK?

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Background and objective: The mechanisms leading to acute cellular rejection (ACR) are not fully understood. B-cell activating factor belonging to the tumor necrosis factor family (BAFF) is a cytokine that enhances B-cell survival and proliferation. The potential role of B-cells in the pathogenesis of ACR has been recently suggested. In this study we aimed to identify abnormalities in serum levels of BAFF (sBAFF) at distinct times before and after heart transplantation (HT) in patients with and without ACR.
Material and Methods: We prospectively evaluated 86 HT (mean age 55 years, 66 male, 20 female). Induction immunosuppressive therapy included 2 doses of anti-CD25 monoclonal antibodies (Daclizumab or Basiliximab). Maintenance immunosuppression included corticosteroids, mofetil mycophenolate and either cyclosporine or tacrolimus. sBAFF (ELISA), assessment points: pre-HT and before and after ACR episodes post-HT. ACR was defined by ISHLT grade 2R or higher.
Results: During 1-yr follow-up, 21 HT (24.4%) developed ACR. Baseline sBAFF was significantly higher in patients who developed ACR as compared with patients who remained free of ACR (1820 $\pm$ 1005 vs. 1320 $\pm$ 93 pg/ml, $p = 0.024$). When we stratified patients according to the median value of sBAFF (cut-off: 1200 pg/ml), survival to ACR was significantly lower in the high baseline BAFF level group (42% vs. 71%, $p = 0.040$). Interestingly, 6 out of 7 patients (86%) with early death (during the first week) disclosed higher baseline sBAFF than patients without ACR ($p = 0.044$). sBAFF levels obtained before and after ACR were 1122 $\pm$ 417 and 1929 $\pm$ 2086 pg/ml respectively ($p = 0.09$). Patients with ACR who disclosed additional abnormal endomyocardial biopsies presented higher baseline BAFF levels than patients without rejection (2253 $\pm$ 970 vs. 1550 $\pm$ 1073 pg/ml, $p = 0.041$).
Conclusion: This is the first study that reports that higher pre-transplant sBAFF concentration might be considered a baseline biomarker for ACR in HT.

BO365 ELEVATED DONOR CARDIAC TROPONIN-I IS NOT ASSOCIATED WITH AN ADVERSE 1-YEAR OUTCOME AFTER HEART TRANSPLANTATION

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Background: We sought to investigate a correlation between donor cardiac troponin-I levels (cTnI), post-transplant graft function and 1-year survival after heart transplantation.
Methods: In a retrospective study data of 83 heart donors, procured in Slovenia between 1st January 2010 and 31st December 2014 and their respective recipients were reviewed. The recipients' data were obtained

through Eurotransplant online database and a written questionnaire sent to the recipient transplant centers. cTnI levels were considered elevated if higher than 0.05 ng/ml.
Results: Elevated cTnI levels were observed in 45 (54%) donors (Group A) and in 38 (46%) donors cTnI remained negative (Group B). The mean troponin level was 0.86 ng/ml in Group A and 0.02 ng/ml in Group B. The two groups did not differ significantly regarding gender (male; 80% in Group A vs. 62% in Group B; $p = 0.14$), donor age (43 $\pm$ 12 years vs. 47 $\pm$ 10 years; $p = 0.10$), arterial hypertension (24% vs. 29%; $p = 0.64$), diabetes (4% vs. 5%; $p = 0.86$), smoking (37% vs. 29%; $p = 0.40$), inotropic support (norepinephrine 0.23 $\pm$ 0.26 mcg/kg/min vs. 0.21 $\pm$ 0.15 mcg/kg/min; $p = 0.72$), left ventricular ejection fraction (53 $\pm$ 12% vs. 57 $\pm$ 11%; $p = 0.11$) or recipient age (53 $\pm$ 11 years in Group A versus 55 $\pm$ 7 years in Group B; $p = 0.39$). Total ischemic time was significantly lower in Group A than in Group B (124 $\pm$ 50 min versus 167 $\pm$ 68 min; $p = 0.004$). Survival analysis showed no difference considering 1-year mortality between the two groups (18% vs. 23%; $p = 0.52$) with graft failure as a cause of death in 7% in Group A and 6% in Group B ($p = 0.76$).
Conclusions: Elevated donor cTnI, especially in combination with shorter ischemic time, does not seem to be associated with inferior graft function and adverse short-term prognosis after heart transplantation. Thus, donor hearts with increased cTnI should not be routinely rejected but may be considered for transplantation on individual basis taking into account specific donor and recipient characteristics.

BO366 CYLEX ASSAY EFFECTIVELY DETECTS IMMUNE ACTIVATION ASSOCIATED WITH GRAFT DYSFUNCTION PHENOTYPE AND DONOR SPECIFIC ANTIBODIES IN HEART TRANSPLAT RECIPIENTS

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Introduction: Reliable characterization of immune function is a crucial but still unmet need for the clinical management of solid organ transplant recipients. The Cylex ImmunoKnow estimates the immune activity by measuring the amount of adenosine triphosphate produced in CD4 cells after stimulation with phytohemagglutinin-I mitogen. However, clinical relevance of its results in heart transplant setting is debated. In addition, while Cylex has been proposed to predict the risk for cellular rejection, its association with antibody-mediated rejection is unexplored.
Methods: We tested for donor HLA specific antibodies (DSA), Cylex, and graft function a series of consecutive patients presenting with signs/symptoms suspect for graft dysfunction (GD) or with clinical stability and normal graft function.
Results: 41 patients were enrolled (59 $\pm$ 13 y, 68% males, at 7 (2–18) y after HT). 32 patients were stable, while 9 presented GD phenotype, with a significantly lower ejection fraction as compared to controls (50 $\pm$ 13 vs. 66 $\pm$ 5%; $p < 0.01$). Overall, 8 patients had de novo DSA (50% in the GD group; $p = 0.04$). Cylex levels were significantly higher in patients with GD phenotype (205[87–371] vs. 60[12–114]ng/ml; $p < 0.01$) or with DSA (211[95–334] vs. 63[13–115]ng/ml $p = 0.01$). Of note, among patients with GD phenotype, high Cylex clustered in the subgroup with DSA. Among patients with no DSA, 12 (36%) reported an infectious episode in the preceding 3 months, showed a significantly lower Cylex level (13[8–78]ng/ml; $p = 0.01$).
Conclusions: This pilot cross-sectional analysis suggests that although based on T-lymphocyte activity Cylex assay revealed high immune activation in patients who developed DSA, and identified GD phenotype. In stable patients, Cylex results indicating low-immune activation were associated with history of recent infection. While confirming the association between Cylex and infectious risk, these data provide novel insights linking CD4 + activation with humoral alloimmunity.

BO367 CARDIAC TRANSPLANT REJECTION CORRELATED WITH NON-INVASIVE PREDICTORS: COMMON CAROTID ARTERY WALL FUNCTIONAL INDICES AND BLOOD LEVELS OF BIOMARKERS

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Background: Allograft rejection would entail an increase in certain blood biomarkers and active substances derived from activated inflammatory cells which could influence on the entire vascular endothelial function and deteriorate arterial wall stiffness.
Aim: To analyze the clinical usefulness of a common carotid wall (CCW) variables as a non-invasive screening for graft rejection in cardiac transplant pts and they correlation with the concentration of biomarkers of cardiac rejection and graft vasculopathy.
Methods: 93 heart transplant recipients were included. CCW rigidity index (iRIG) was estimated using empirical equation: iRIG = ((Vs-Vd)/aT)*(Dd2/(Dd2-Ds2)), where Vs, Vd, Ds, and Dd are systolic and diastolic common carotid artery blood flow velocities and diameters, and aT is carotid flow acceleration time. Non-invasive evaluation was performed on the day of the endomyocardial biopsy. The concentration of pregnancy-associated plasma protein-A (PAPP-A), placental growth factor (PlGF), sCD40L, and sCD30 was measured by ELISA.
Results: Antibody-mediated (AMR) and acute cellular rejection (ACR) were found in 22 (23.7%) and 17 (18.3%) recipients. Mean iRIG in pts without rejection was lower in comparison to AMR and ACR (5514.7 $\pm$ 2404.0 vs. 11856.1 $\pm$ 6643.5 and 16071.9 $\pm$ 10029.1 cm/sec2, $p = 0.001$). AUC for iRIG was 0.90 $\pm$ 0.03 units2. iRIG values above estimated threshold 7172 cm/sec2 suggested RR of any type of rejection 17.7 (95%CI = 6.3–49.9) sensitivity 80.5%, specificity – 81.1%. iRIG was not correlated with gender, age, plasma levels of PAPP-A, and PlGF, but correlated with level of sCD30 before and one year after THx ($p < 0.05$, $p < 0.02$); and with plasma level of sCD40L one year after THx, $p < 0.05$.
Conclusions: Non-invasive measurement of carotid artery wall rigidity index with triplex ultrasound and blood levels of sCD30 and sCD40L may be a simple screening tool for rejection risk stratification.

BO368 SERUM LEVELS OF VEGF-A AND PLGF-1 BUT NOT VEGF-D ARE ASSOCIATED WITH ACUTE CELLULAR REJECTION IN HEART TRANSPLANT RECIPIENTS

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Background: Acute cellular (ACR) and antibody mediated (AMR) rejections are important limitations for the long-term survival of heart transplant recipients. The aim was to analyze the relationship between the levels of the vascular endothelial growth factors (VEGF-A, VEGF-D and placental growth factor PlGF-1) and risk development of ACR and AMR of the cardiac allografts.
Methods: 103 heart transplant recipients, 85 (82.5%) male, aged 47 $\pm$ 14 years were followed up 366 $\pm$ 278 days after heart transplantation (HTx). VEGF-A, VEGF-D, PlGF-1 serum concentration was determined by magnetic bead-based quantitative multiplex assay, using Luminex 200 device.
Results: The median concentration of VEGF-A in patients before HTx was 638.95 [268.67–959.09] pg/ml, VEGF-D – 41.01 [17.84–100.35] pg/ml, PlGF-1 – 3.35 [1.00–6.86] pg/ml. After HTx level of VEGF-A was lower – 199.14 [109.93–432.43], $p = 0.001$. There were no correlations between levels VEGF-A, VEGF-D and PlGF-1 with age, gender and diagnosis. ACR was found in 17 pts., AMR – in 19 recipients. After HTx VEGF-A level was higher in recipients with ACR than to those without them ($p = 0.001$). In patients with VEGF-A $\geq$ 199 pg/ml relative risk of ACR was 7.1 $\pm$ 0.7, AUC = 0.779 (95% CI 0.7–0.9, $p = 0.000$). After HTx PlGF-1 level was higher in recipients with ACR too ($p = 0.039$). In patients with PlGF-1 $\geq$ 4.8 pg/ml relative risk of ACR was 1.8 $\pm$ 0.5, AUC = 0.65 (95% CI 0.5–0.8, $p = 0.048$). There were no correlations between VEGF-D level with ACR and all three biomarkers with AMR.
Conclusion: Serum levels of VEGF-A and PlGF-1 after HTx may be regarded as indicators of increased risk of ACR.

BO369 EFFECTS OF MILD HYPOTHERMIA APPLIED DURING EARLY REPERFUSION ON CARDIAC HEMODYNAMIC RECOVERY AFTER GLOBAL ISCHEMIA IN AN ISOLATED RAT HEART MODEL OF DONATION AFTER CIRCULATORY DETERMINATION OF DEATH

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Background: Cardiac graft availability is currently insufficient to meet transplantation demand, but could potentially be improved with donation after circulatory determination of death (DCDD). In DCDD heart transplantation, interventions before warm ischemia are limited; however, cardioprotective strategies, including physical or pharmacological approaches, may be applied at the time of procurement to limit or reduce graft injury. Therefore, we investigated whether mild hypothermia, applied during the first minutes of reperfusion improved heart recovery after warm ischemia.
Methods: Isolated hearts of male Wistar rats were perfused in working-mode (37°C) with modified Krebs-Henseleit buffer for 20 min, then subjected to global ischemia for 27 min (37°C) and 60 min reperfusion. Mild hypothermia (30°C; MH) was applied during the first 10 min reperfusion. Temperature was then increased to 37°C over 5 min. Hemodynamic and biochemical parameters were monitored. Data (mean±SD) were compared using t-tests; p-values were corrected for multiple comparisons.
Results: Recovery of left ventricular work (developed pressure*heart rate) expressed as a percentage of pre-ischemic values was higher in MH versus

control hearts (after 20 min: 47.5 ± 6.0% versus 31.0 ± 8.1% ($p < 0.05$), after 40 min: 54.9 ± 2.3% versus 43.8 ± 5.2% ($p < 0.05$) and after 60 min 62 ± 5% vs. 50 ± 7% ($p < 0.06$), respectively, $n = 4–5$). Preliminary results indicate that improved hemodynamic recovery was accompanied by reduced release of necrosis markers (lactate dehydrogenase and troponin-T) and lactate during the first minutes of reperfusion.
Conclusions: In DCDD heart transplantation, strategies applied at graft procurement, such as mildly hypothermic reperfusion, could positively impact on cardiac recovery and potentially limit graft injury. Further investigation is required to identify optimal reperfusion strategies to facilitate the use of DCDD cardiac grafts.

BO370 CARDIAC MICRORNA (MIRNA) EXPRESSION AFTER ISCHEMIA AND REPERFUSION IN AN ISOLATED RAT HEART MODEL OF DONATION AFTER CIRCULATORY DETERMINATION OF DEATH (DCDD)

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Background: The lack of donor organs is a key limiting factor in heart transplantation as conventional cardiac grafts, obtained through donation after brain death, cannot fulfill the growing demand. DCDD hearts may be an option, although the inevitable period of warm ischemia followed by reperfusion (I/R) may induce irreversible tissue damage that could prevent transplantation.miRNA, small, non-coding molecules, are important master regulators of key cellular processes in I/R injury, such as apoptosis, calcium overload and energy metabolism. We investigated changes in cardiac miRNA expression during the first minutes of reperfusion following global ischemia, and their possible association with markers of post-ischemic recovery.
Methods: Isolated, working hearts of 38 adult, male Wistar rats underwent baseline perfusion, followed by 27 min normothermic, global ischemia, and 10 min reperfusion. Left ventricular tissue was harvested from three experimental groups: "End Baseline" (EB), "End Ischemia" (EI), and "End Reperfusion" (ER). Expression of miR-1-3p, miR-15b-5p, miR-20a-5p, miR-21-5p, miR-24-3p, miR-101b-3p, miR-133a-3p, miR-145-5p, miR-199a-5p, miR-223-3p, miR-320-3p, miR-494-3p and miR-499-5p were measured by RT-qPCR. Hemodynamic and biochemical parameters were also monitored.
Results: Expression was significantly reduced for miR-20a-5p at ER compared to EB and EI, and for miR-1-3p at ER compared to EB ($p < 0.01$ for all). At ER, expression levels for almost all miRNA correlated with previously identified markers of post-ischemic hemodynamic recovery.
Conclusion: We demonstrate that expression of two cardiac miRNA, both involved in apoptosis, rapidly drops during global ischemia and early reperfusion, thereby supporting an early, regulatory role in I/R injury. In addition, early reperfusion expression levels of several miRNA provide information regarding post-ischemic hemodynamic recovery, thus rapid miRNA profiling may help to judge DCDD graft suitability.

013 IMMUNOBIOLOGY/BASIC SCIENCE

BO371*

DNA METHYLATION OF THE IFNγ PROMOTER IN CD8 + T CELL SUBSETS IS MODULATED BY CMV INFECTION BUT NOT BY ALLOREACTIVITY IN KIDNEY TRANSPLANTATION PATIENTS

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Background: DNA methylation plays a critical role in the function of cells, including cells of the immune system. Little is known about the methylation status of immune related genes in relation to viral infections and alloreactivity. Here we studied the methylation status of the pro-inflammatory cytokine IFNγ in relation to CMV infection and rejection in kidney transplantation patients.
Methods/Materials: The DNA methylation status of two regulatory CpGs (CpG-186 and CpG-54) in the IFNγ promoter was determined by pyrosequencing in FACS sorted naïve, central memory (CM), effector memory (EM) and EMRA CD8 + T cells of CMV-seropositive and CMV-seronegative donors and before, 3 months and 12 months after transplantation in CMV-seronegative patients. Both patients who developed a biopsy proven acute rejection (rejectors) and patients who remained free from rejection (non-rejectors) were included.
Results: A clear-cut difference was seen between the IFNγ methylation in naïve CD8 + T cells (CMV-seronegative donors, CpG-186 and CpG-54, median with range: 65% (53–71) and 79% (65–83)) and the memory CD8 + T cell subsets (CM: 13% (8–17) and 17% (10–21); EM: 6% (5–13) and 8% (7–20); EMRA: 2% (2–6) and 2% (2–9)). The IFNγ methylation status inversely correlated with the % of IFNγ producing cells. Before transplantation the IFNγ methylation was comparable to the methylation status in CMV-seronegative donors and did not significantly change during the first year after transplantation. Comparing rejectors and non-rejectors did not demonstrate significant differences. In contrast to alloreactivity, CMV infection significantly ($p < 0.05$) decreased the % of methylation of both CpGs in the naïve, CM and EM CD8 + T cells.
Conclusion: Chronic kidney disease, the transplantation procedure itself and subsequent alloreactivity does not modulate the methylation status of IFNγ, while CMV infection significantly decreases the methylation status of IFNγ in CD8 + T cells.

BO372

A PRIMARY CYTOMEGALOVIRUS INFECTION POST-TRANSPLANTATION HAS A SIGNIFICANT IMPACT ON CIRCULATING T CELLS AND RENAL ALLOGRAFT FUNCTION

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Erasmus MC

Background: Cytomegalovirus (CMV)-infection may profoundly affect the peripheral T-cell compartment and is associated with T-cell ageing and generation of cytotoxic CD4 + CD28null T cells. We investigated the effect of a primary CMV-infection post-kidney transplantation (KT) in CMV-seronegative recipients receiving a kidney from a CMV-seropositive donor (D+/R-) on peripheral T cells under immunosuppression and valganciclovir prophylaxis.
Methods: Within the first year post-KT, the presence of CMV-specific T cells and T-cell differentiation status were monitored. In addition, as T-cell ageing parameters we measured the T-cell receptor excision circle (TREC)-content, CD31 + naïve T-cell numbers and the relative telomere length (RTL). The D+/R- KT-recipients were compared to recipients of a D+/R+ combination.
Results: Eleven out of the 22 included D+/R- recipients had a CMV-viremia post-KT. Only in the viremic patients a significant impact of CMV-infection on T cells was observed. They developed CMV-specific, (IFNγ+)CD137-expressing CD4 + and CD8 + T cells and their T-cell compartment shifted towards more differentiated memory cells with expansion of CD4 + CD28null and CD8 + CD28null T cells. One year post-KT the total CD8 + T-cell count was almost doubled in this group compared to non-viremic D+/R- and D+/R+ recipients. Both the TREC-content ($p < 0.01$) and CD31 + naïve CD4 + ($p = 0.01$) and CD8 + ($p = 0.05$) T-cell numbers were significantly decreased at 12 months post-KT. The RTL of CD8 +, but not CD4 + T cells significantly ($p = 0.03$) declined in the D+/R- KT-recipients post-KT. The viremic D+/R- patients had a significant ($p = 0.04$) lower glomerular filtration rate compared to D+/R+ KT recipients at 12 months post-KT.
Conclusion: A primary CMV-infection impacts peripheral T cells by enhancing T-cell ageing and is associated with a poorer allograft function.

BO373

DEFICIENCY OF NATURALLY OCCURRING ANTI ANGIOGENIC ANTIBODIES ASSOCIATES WITH THE DEVELOPMENT OF METASTATIC CANCER POST RENAL TRANSPLANT

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We assessed the presence of naturally occurring blocking antibodies to mediators of vascularisation and metastasis in Kidney Transplant Recipients (KTR) with metastatic cancer ($n = 11$), non metastatic cancer ($n = 32$) and 38 KTR with no cancer history and 195 healthy controls. The antibodies assessed were: PAR1-antibody, VEGF-A-antibody, VEGF-Receptor 1 antibody, VEGF-B antibody, VEGF-Receptor 2-Ab, EGF-Antibody and EGFR-AntibodyAll KTR had stable graft function and there were no differences in immunosuppressive regimens, HLA mismatch, or duration of immunosuppression between KTR groups. KTR with metastatic cancer were significantly older than those without cancer ($p = 0.011$). KTR with non metastatic cancer were similar in age to KTR without cancer ($p = 0.071$). There was no correlation with age to any of the antibodies tested. Compared to healthy controls KTR without cancer had lower levels of PAR1-ab, VEGF-R1-Ab, VEGF-B-Ab, EGF-Ab and EGFR-Ab (all p values<0.001). However KTR had similar levels VEGF-A-Ab and VEGF-R2-Ab. KTR with non metastatic cancer had similar antibody profiles to those KTR without cancer apart from having lower levels of PAR1-abs ($p = 0.043$). KTR with metastatic cancer had lower levels of antibodies to PAR1, VEGF and its receptors (all p values<0.05) compared to those with no cancer history. Levels of antibodies to EGF and its receptor were similar between all KTR groups. These data show that KTR have lower levels of antibodies to mediators of tumour vascularisation compared to healthy controls. The reason for this is unknown but may relate to immunosuppression. KTR with metastatic cancer had further reduction in antibodies to PAR1 and the VEGF pathway but not EGF pathway. We are assessing stored serum samples to confirm whether KTR with metastatic cancer lose these antibodies during the development of cancer or whether they historically had low levels. It is possible these antibodies could risk stratify KTR at risk of developing metastatic cancer.

BO374

REDUCED AUTOPHAGY CORRELATES WITH INCREASED APOPTOSIS IN THE KIDNEY, BUT NOT IN THE LIVER, OF BRAIN-DEAD RATS

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Donation after brain death (BD) leads to inferior graft quality compared to living donation. BD increases apoptosis, which can normally be counteracted by autophagy. Whether autophagy is affected after BD is unknown. This study investigated the role of autophagy in the BD setting by looking at the interplay between autophagy, apoptosis, and tissue injury in the liver and kidney of brain-dead rats.

BD was induced in mechanically ventilated rats by inflation of a Fogarty catheter in the epidural space. After 4 h of BD, plasma, kidney, and liver tissue were collected. Routine biochemistry was performed to assess injury and function of the liver and kidney. Autophagy (p62, Beclin 1, and LC3I/II), apoptosis (cleaved caspase 3, Bax), and mTOR activity (phospho-S6) markers were analysed with Western blotting and qPCR.

Brain-dead animals had increased AST, ALT, creatinine, and urea levels. In the kidney, BD reduced levels of autophagic marker LC3-II, which is associated with increased activation of autophagy-inhibitor mTOR. Moreover, decreased LC3-II significantly correlated with increased autophagy degradation substrate p62 and apoptosis marker cleaved caspase 3 (cC3). Bax and Beclin 1 protein levels remained unaltered, although Beclin 1 mRNA expression was significantly decreased. In the liver, BD increased gene expression of Bax as well as cC3 expression. However, protein levels of increased apoptosis or affected autophagy were not observed on a protein level.

BD causes tissue injury in the liver and kidney of brain-dead rats. However, BD had differential effects on autophagy. In the kidney, increased apoptosis significantly correlates with decreased autophagy and points to an anti-apoptotic, protective role for autophagy after BD. Yet, autophagy was not significantly altered in the liver. As such, these results suggest a possible role for autophagy in protection against BD-induced kidney damage.

BO375 ROLE OF KIDNEY DONOR'S INFLAMMATORY STATUS IN M2 MACROPHAGE ACTIVATION AND FIBROSIS

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Background: Kidneys from living donors (LD) show better graft and patient outcome than deceased ones (DD). Little is known about the inflammatory state of kidney donors at the time of donation and how it may influence chronic graft dysfunction and interstitial fibrosis and tubular atrophy (IFTA). Macrophage infiltration in the renal tissue could be related with graft outcome and IFTA. We previously showed that circulating monocytes could be involved in the prognostic of living kidney recipients and that it could be indicative of early onset of fibrosis.
Methods/Materials: We collected 67 samples of pre-implant renal tissue, 34 from LD and 33 from DD. Samples were homogenized and mRNA was extracted to obtain cDNA. It was processed in TaqMan® OpenArray® Real-Time PCR Plates to analyse the mRNA expression of 160 genes.
Results: Pannexin is increased in DD respect to LD ($p = 0.0108$). The ATP released through this channel could activate monocytes and macrophages via purinergic receptors. The augmented expression of CD14 ($p = 0.048$), CD163 ($p = 0.0146$) in DD indicates a larger number of M2 macrophages than in LD. We also found a correlation between pannexin and the M2 marker CD206 ($r = 0.5147$, $p = 0.0031$). Moreover, TGF-β1, the main inducer of fibrosis that is secreted by M2 macrophages, is increased in DD ($p = 0.0459$) and correlates with the adenosine transporter ENT1 ($r = 0.7187$, $p < 0.0001$). The expression of this transporter also correlated with the adenosine receptor A2A ($r = 0.6365$, $p < 0.001$), which in turn has been associated with fibronectin levels ($r = 0.7477$, $p < 0.0001$).
Conclusion: Infiltrating M2 macrophages in renal tissue of DD could induce graft fibrosis through an increase of extracellular adenosine and TGF-β1. This role of the inflammatory status of DD has not been previously explored.

BO376 RECIPIENT NATURAL KILLER CELL ALLORECOGNITION OF PASSENGER DONOR LYMPHOCYTES AND ITS EFFECT ON ADAPTIVE ALLOIMMUNITY AFTER TRANSPLANTATION

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Background: Memory T cells reside in non-lymphoid tissue but how their presence in solid organ allografts impacts upon outcomes is unknown. We have previously described how graft-versus-host (GVH) allorecognition by passenger CD4 T cells within MHC Class II-mismatched bm12 heart grafts provokes humoral autoimmunity in B6 recipients. Here we aimed to examine how such GVH recognition impacts upon alloresponse to more mismatched allografts
Methods: An MHC class I and II mismatched murine model of cardiac transplantation was developed (bm12.Kd.IE to B6). Following transplantation, cellular and humoral responses were assayed and the impact of GVH recognition assessed by depleting donor CD4 T cells prior to graft procurement
Results: Bm12.Kd.IE heart grafts provoked strong germinal centre allo- and auto-antibody responses in B6 recipients and developed vasculopathy. In contrast, heart grafts from CD4 T cell-depleted donors developed only minimal vasculopathy, alloantibody responses were weaker without observable autoantibody. Bm12.Kd.IE CD4 T cells survive long term when transferred to RAG hosts suggesting avoidance of host NK cell killing may be essential for autoantibody development. In support, in a model of alloantibody mediated vasculopathy, depletion of NK cells from a B6 recipient of a BALB/c heart graft resulted in the development of autoantibody, amplification of the alloantibody response and rapid rejection. This amplification was abrogated by depleting donor CD4 T cells
Conclusions: Although host adaptive immunity is expected to effect destruction of passenger lymphocytes within heart allografts, this occurs too slowly to prevent GVH-mediated augmentation of the alloresponse to the graft. Rapid killing of donor lymphocytes by host alloreactive NK cells is instead essential. Passenger CD4 lymphocytes may therefore contribute to chronic rejection in recipients who receive an allograft that does not prompt innate NK cell recognition

BO377 EOMES-EXPRESSING CD8 + T CELLS AND TH17 CELLS MEDIATE RESISTANCE TO COSTIMULATORY BLOCKADE IN MICE

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Background: Costimulatory blockade-resistant rejection remains an obstacle to tolerance induction and long-term graft survival. The purpose of this study was to evaluate the responsiveness of distinct CD4 + and CD8 + T cell subsets to costimulatory blockade.
Methods: We used mice genetically deficient for hallmark T cell transcription factors such as B6.RORγt knockout (KO) mice, B6.T-bet KO mice, and B6.RORγt-T-bet double-KO mice. Purified T cells from these mice and wt controls were adoptively transferred into B6.Rag-common-γc DKO recipients of fully mismatched Balb/c skin allografts (STx) ± treatment with CTLA4Ig and MR-1.
Results: Untreated controls from all mouse strains promptly rejected their grafts with similar kinetics but different cytokine profiles. RORγt KO T cell recipients featured a Th1-mediated rejection (55% IFN-γ+ T cells) while T-bet KO T cell recipients rejected with a Th17/Th2-driven phenotype (15% IL-17 +, 28% Gata-3 + T cells). Importantly, DKO T cell recipients were characterized by a Th2-driven rejection (42% Gata-3+ T cells). Next, we tested whether T cell subsets respond differently to costimulatory blockade. Importantly, RORγt KO recipients showed prolonged allograft survival (MST 76d) upon treatment, whereas T-bet KO and DKO STx recipients rejected promptly like untreated controls (22d, 27d, respectively). Critically, Th1, but not Th17 alloresponses were significantly suppressed by costimulatory blockade as indicated by flow cytometry and ELISA. Moreover, we found that DKO T cell recipients failed to mount an alloreactive Th2 response under costimulatory blockade conditions. Instead, we detected significantly higher numbers of Eomes+CD8 + T cells in the rejecting DKO recipients when compared to RORγt or T-bet single KO mice.
Conclusion: While Th1 and Th2 cell-mediated alloresponses may be responsive to costimulatory blockade, Th17 and Eomes+Tc cell-mediated alloresponses seem to drive costimulatory blockade-resistant allograft rejection in mice.

BO378 SH2B ADAPTORS ARE REGULATORY SIGNALING PROTEINS CONTROLLING MICROVASCULAR INFLAMMATION UPON ANTIBODY-MEDIATED REJECTION OF CARDIAC TRANSPLANTS

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Understanding molecular mechanisms and signaling induced by donor-specific antibodies (DSA), complement and inflammation during antibody-mediated rejection (AMR) is required for improved diagnosis and graft survival. We previously reported on the regulatory functions of SH2B3/Lnk protein toward inflammation and EC dysfunction. The present study investigated the expression of adaptor proteins of the SrcHomology2B family (SH2B1, SH2B2 and SH2B3) in cardiac tissue and leukocyte subpopulations and their regulation upon acute AMR in human heart transplant biopsies. SH2B adaptors were analyzed by QPCR and immunohistochemistry in purified leukocyte subsets and in endomyocardial biopsies (EMB) from non failing transplants ($n = 13$) or transplants with AMR (pAMR2/3; $n = 9$). First, we found that in normal cardiac tissue, basal SH2B1 and SH2B2 is low and mostly restricted for SH2B1 to microvascular ECs with a nuclear localization. Basal SH2B3 is predominant in cardiomyocytes and macrovascular ECs. AMR associates with a significant upregulation for SH2B1 and SH2B2 in transplant microvascular inflammation at with a staining in both vascular cells and infiltrating CD68 + macrophages. AMR also correlates with change in SH2B3, primarily in cardiomyocytes. In AMR, SH2B2 and SH2B3 regulation in the grafts showed individual variations suggesting a mutually exclusive regulation for these two SH2B. Moreover, we provide first evidence for a role of SH2B3 in cardiomyocyte and for anti-HLA class II DSA being an effector of SH2B regulation in AMR. Overall, SH2B proteins are strongly expressed in microvascular inflammation during acute AMR suggesting a specific regulatory action of SH2B in EC activation and macrophage differentiation. Imbalance between SH2B2 and SH2B3 needs confirmation to determine whether the increase in SH2B2 and B3 in these grafts could be a predictive marker of graft survival and / or therapeutic target for the control of microvascular inflammation and EC dysfunction.

BO379 EXOGENOUS LIPOCALIN-2 RESCUES KIDNEY ALLOGRAFT FROM ACUTE INJURY IN A MURINE MODEL OF RENAL TRANSPLANTATION

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Background: Lipocalin-2 (Lcn2), rapidly produced by damaged nephron epithelia, is one of the most promising new markers of renal injury, delayed graft function, and acute allograft rejection (AR). Discrepancy exists about the role of Lcn2 in renal injury, whereas its role in the renal AR has not been demonstrated so far. Determination of Lcn2 function during renal AR could provide new therapeutic options for both application of recombinant Lcn2 or its blockade.
Methods: To understand the role of Lcn2 in renal AR, kidneys from Balb/c mice were transplanted into C57Bl/6 (wt and Lcn2-/-) mice and analyzed for morphological and physiological outcomes of AR at post-transplantation days 3, 5 and 7. To estimate allograft function serum creatinine, urea and Lcn2 were measured. Tissue sections were stained with HE and PAS and evaluated according to the Banff criteria. Expression of Lcn2 and cytokines was measured by RT-qPCR and IHC analysis. Cell death was assessed by immunostaining the graft tissues with cleaved Caspase-3 antibody and TUNEL staining.
Results: The allografts showed a steady increase in intensity of interstitial infiltration, tubulitis and periarterial aggregation of lymphocytes over the course of 7 days, associated with a substantial elevation in serum levels of creatinine, urea and Lcn2. No significantly differences between the allografts of C57Bl/6 wt and Lcn2-/- recipients were observed. However, perioperative administration of recombinant Lcn2 (rLCN):siderophore:Fe complex (250 mg) to the recipeient or daily immunosuppression with CsA (10 mg/kg BW) prevented histomorphologically proven severe acute allograft rejection and rescued the allograft function. Histochemical analyses of the allografts showed reduced caspase-3 activation and less number of TUNEL positive cells in the recipients treated with rLCn2 or CsA.
Conclusion: Lcn2 plays an important role in preventing kidney allograft injury, suggesting its therapeutic potential in transplantation medicine.

BO380 HIGH DOSES OF M-TOR INHIBITORS MAY INDUCE PULMONARY PRO-FIBROTIC EFFECTS IN RENAL TRANSPLANT RECIPIENTS: RESULT OF A TRANSLATIONAL COMPARATIVE RESEARCH APPROACH BETWEEN PROGRAF VERSUS EVEROLIMUS

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Background: Several studies have reported an high rate of pulmonary fibrosis-associated adverse effects (including Bronchiolitis obliterans organizing pneumonia) in patients treated with mTOR inhibitors, immunosuppressants widely used in renal transplant patients. It has been suggested that epithelial to mesenchymal transition (EMT) in airway cells may determine this condition. However, at the moment, the exact biological machinery involved is not completely clarified.
Methods: To assess this research objective, we performed a translational study. First we analyzed the *in vivo* pulmonary pro-fibrotic potential of Everolimus (EVE) by computing a pulmonary fibrosis index score (PFIS), obtained by the combination of several computerized tomography, hemogasanalytic and spirometric parameters, in 12 renal transplant patients in EVE maintenance immunosuppressive treatment and 14 patients treated with Advagraf (ADV). Subsequently, we carried out an *in vitro* study in which we assessed whether EVE (5, 10, 100 nM) or Prograf (5 nM, 500 nM e 5 μM) was able to induce EMT in bronchial epithelial cells (Nuli-1) and human type II pneumocyte-derived A549 cell line.
Results: In the *in vivo* part of the study, we found that the pulmonary fibrosis index was higher in EVE-treated patients compared to those treated with ADV (mean±SD 2.58 ± 1.83 versus 1.21 ± 1.25, p value 0.03). This effect was positively correlated to the trough levels in EVE-treated patients ($R2 = 0.35$). Interestingly, only high doses of EVE were able to induce up-regulation of alpha-SMA, Fibronectin and Vimentin at gene-expression and protein level in A549. No effects were seen in Nuli-1.
Conclusions: All together, our data revealed that high doses of EVE may induce pulmonary fibrosis and that this effect could be mediated by EMT in pnemocyte cells.

019 ISCHEMIA/REPERFUSION INJURY/PRESERVATION

BO381 AMELIORATION OF RENAL POSTISCHEMIC INJURY BY DEHIDROEPIANDROSTERONE AND BY THE ANTIDEPRESSANT FLUVOXAMINE

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Introduction: We previously showed that renal ischemia/reperfusion injury (IRI) is more severe in males versus females, and sex hormones may be responsible for the difference. Dehidroepiandrosterone (DHEA) is protective in IRI: not only on estrogen- and androgen-, but also on Sigma-1 receptor (S1R). The antidepressant fluvoxamine (FLU) has a greater affinity to S1R than DHEA.
Aim: To examine the effect of DHEA and FLU, and the role of S1R in a rat model of renal IRI.
Methods: We used male Wistar rats after 50 min renal IRI. To examine the S1R-agonistic effect of DHEA rats were pretreated 25 and 1 h before ischemia with (1) DHEA-sulfate sc. or (2) DHEA+S1R antagonist NE100. The administration of (3) FLU ip. or (4) FLU+NE100 30 min. before ischemia was used to evaluate the renoprotective effect of FLU. IRI rats treated with vehicle (VEH) and sham-operated ones (C) served as controls (n = 6/group). We also examined postischemic survival (n = 6/group), and the decrease of renal function 24 h after reperfusion. Changes in renal capillary diameter and structural damage were evaluated with *in vivo* multifoton microscopy, histological injury was examined in PAS stained slides, semiquantitatively.
Results: Both DHEA and FLU pretreatment increased postischemic survival and ameliorated renal structural and functional damage (BUN, mmol/l: C:7.12 ± 0.12; VEH:46.42 ± 0.96; DHEA:39.6 ± 0.81; DHEA+NE100:44.13 ± 2.13; FLU:40.48 ± 0.87; FLU+NE100:54.13 ± 3.06). Vasoconstriction induced by IRI was prevented by both DHEA and FLU, whereas NE100 inhibited their effect (capillary diameter, μm): C:9.86 ± 1.23; VEH:7.48 ± 0.11; DHEA:8.48 ± 0.09; DHEA+NE100:7.6 ± 0.08; FLU:10.64 ± 2.53; FLU+NE100:7.88 ± 1.67).
Conclusion: Both endogenous S1R agonist DHEA and exogenous FLU increase survival and are renoprotective in renal IRI. FLU already used as an antidepressant with few side effects might be a promising agent in states with renal IRI, especially in pre- and posttransplant therapy.
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BO382 EFFECTS OF ENDOTHELIN RECEPTOR ANTAGONISM IN AN EXPERIMENTAL MODEL OF RENAL TRANSPLANTATION

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Background: Uncontrolled Donation after Circulatory Death (uDCD) donors provide a large potential source of kidneys but there is reluctance to use them due to prolonged warm ischaemic times. Endothelin-1 is a major contributor to ischaemic injury through its vasoconstrictive and proinflammatory effects. This study aimed to investigate the benefit of endothelin receptor blockade in an experimental model of uDCD transplantation.
Methods: Porcine kidneys underwent 60 min warm ischaemia and 2 h cold ischaemia followed by 3 h of reperfusion with autologous blood without (control, n = 6) and with (n = 6) 500 μg BQ-123, a selective ETA endothelin receptor antagonist [Sigma-Aldrich®]. Perfusion parameters were recorded continuously and blood, serum, urine and tissue samples taken at fixed intervals to analyse markers of renal function, injury and inflammation.
Results: Renal blood flow was significantly higher in the experimental group at 15–30 min of reperfusion (29.6–37.7 vs. 13.1–18.2 ml/min/100 g, p = 0.02), after which, although higher throughout, statistical significance was lost.

Urine output, creatinine clearance and oxygen consumption were also higher in the experimental group throughout reperfusion but statistical significance was only seen in the 1st hour urine output (83 vs. 32 ml/hr, p = 0.01).

Urinary Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels were not different between the groups (p = 0.18). Urinary endothelin-1 was significantly lower in the experimental group (7.3 vs. 19.4 pg/ml, p = 0.02).

There was no difference in levels of urinary Interleukin-6 and Tumour Necrosis Factor-α between the groups (p = 0.27 and 0.21 respectively).
Conclusion: Kidneys can recover from warm ischaemic injury. BQ-123 appeared to improve perfusion & function initially and the lower endothelin-1 levels suggest reduced tubular injury. However, a sustained or significant overall functional benefit was not seen.

BO383 IMPACT OF ADAMTS13, VON WILLEBRAND FACTOR-CLEAVING PROTEASE, ON HEPATIC ISCHEMIA/REPERFUSION INJURY

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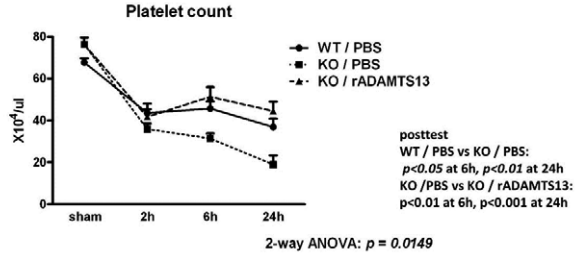
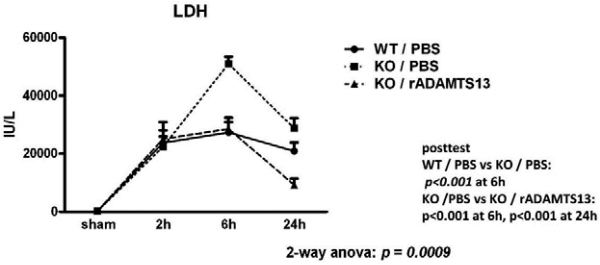
Background: Multimeric von-Willebrand factor (vWF) is a well-known central player not only in physiological hemostasis but also in various pathological disorders with intravascular coagulation. Here we report the impact of a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13 (ADAMTS13), the cleaving protease of vWF multimers, on hepatic ischemia/reperfusion injury (IRI).
Materials and Methods: Male ADAMTS13 knockout (KO) and corresponding wild-type (WT) mice (8–10 weeks-old) were exposed to 70% partial hepatic ischemia for 90 min followed by either vehicle (WT + vehicle and KO + vehicle) or recombinant ADAMTS13 administration (KO + rADAMTS13) twice, prior to ischemia and just before reperfusion. After reperfusion, hepatic microcirculation, peripheral platelet counts, transaminase release, lactate dehydrogenase (LDH), liver histology and proinflammatory cytokines and chemokines expressions were examined.
Results: After 24 h of reperfusion, hepatic microcirculation in KO fell down to 33.1% of the pre-ischemic value, which was significantly lower than in WT (69.8%, p < 0.01). Of interest, rADAMTS13 improved such microcirculatory failure up to 67.4% (p < 0.01). CD42b immunohistochemistry revealed massive platelet aggregation within hepatic sinusoids in KO, which was markedly improved by rADAMTS13 administration. Consequently, platelet counts (p = 0.0149), ALT (p = 0.0032), LDH (p = 0.0009), were all significantly deteriorated in KO, but almost completely ameliorated by rADAMTS13 administration (Fig. 1).

Figure1





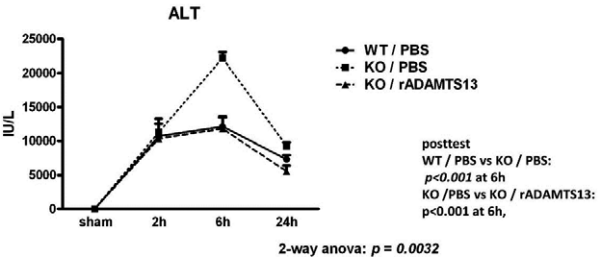
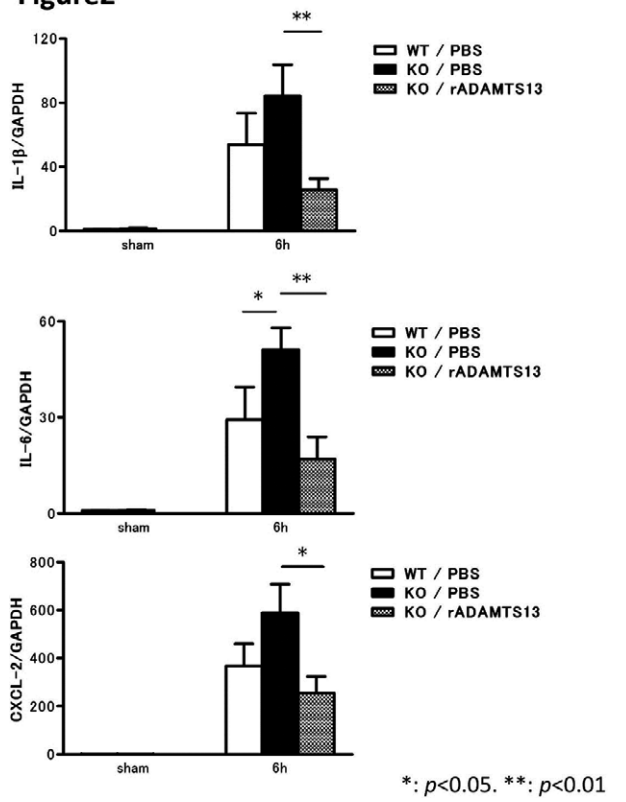


Figure2



In view of subsequent inflammatory response, IL-1b, IL-6, and CXCL-2 production were all amplified after hepatic IRI, which were, however, all alleviated by rADAMTS13 supplementation, as summarized in Fig. 2.
Conclusion: ADAMTS13 plays a considerable role not only in maintaining hepatic microcirculation but also in attenuating subsequent inflammatory cascades, thus providing a novel therapeutic approach against hepatic IRI.

BO384

SIRT1 AND HIGH MOBILITY GROUP BOX 1 IN STEATOTIC AND NON STEATOTIC LIVER PRESERVATION

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Background: Sirtuin 1 (SIRT1) is a NAD+-dependent histone deacetylase that regulates various pathways involved in ischemia-reperfusion injury (IRI),. Moreover, high mobility group box 1 protein (HMGB1) has also been involved in inflammatory processes during IRI. However, both SIRT1 and HMGB1 role in liver preservation is poorly understood. In this communication, we evaluated the potential relationship between SIRT1 and HMGB1 in steatotic and non-steatotic liver grafts preserved in IGL-1 preservation solution enriched or not with trimetazidine (TMZ).
Methods/Matherials: Steatotic and non-steatotic livers were preserved in IGL-1 preservation solution (24 h, 40 C) enriched or not with TMZ (10–6 M), and then submitted to "ex-vivo" reperfusion (2 h; 37C). Liver injury (AST/ALT), and function (bile output, vascular resistance) were evaluated. SIRT1, HMGB1, autophagy parameters (beclin-1, LC3B), PPARgamma and heat shock proteins (HO-1, HSP70) expression were determined by western blot. Also we assessed oxidative stress (MDA), mitochondrial damage (GLDH) and TNF-a levels.
Results: Elevated SIRT1 and enhanced autophagy were found after reperfusion in steatotic livers preserved in IGL-1 + TMZ when compared to IGL-1. However, these changes were not seen in case of non-steatotic livers. Also, HO-1 increases in IGL-1 + TMZ group were evident only in case of steatotic livers, whereas HSP70 and PPAR-gamma proteins expression were enhanced only in non-steatotic ones. All reported changes were consistent with decreased HMGB1 levels, liver injury diminution, ameliorated hepatic function, as well as decreased TNF-alpha levels. In addition, the oxidative stress and mitochondrial damage were efficiently prevented by the IGL- 1 + TMZ use.
Conclusions: SIRT1 is associated with HMGB1 decreases and increased autophagy in steatotic livers, contributing to increased tolerance to cold IRI.

BO385

ACETAZOLAMIDE PROTECTS STEATOTIC LIVER AGAINST COLD ISCHEMIA REPERFUSION INJURY

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Background: Steatotic livers are more vulnerable to ischemia reperfusion injury (IRI) than non steatotic ones due to the exacerbated oxidative stress and microcirculation alterations. Acetazolamide (AZ), a carbonic anhydrase (CA) inhibitor and diuretic agent, has been used in many hypertensive-related diseases and has been shown to protect kidney against IRI. In our study, we investigate whether AZ administration could protect steatotic livers against IRI as well as the possible associated mechanisms.
Methods/Materials: Obese Zucker rats livers were preserved in Institut Georges Lopez (IGL-1) storage solution for 24 h at 4°C and then subjected to a "ex vivo" perfusion for 2 h at 37°C. Alternatively, rats were treated with intravenous injection of AZ (30 mg/kg) before liver recovery. Liver injury (AST/ALT, histology), hepatic function (bile production, bromosulfophtalein (BSP) clearance) and vascular resistance were determined. We assessed endothelial nitric oxide synthase (eNOS), mitogen activated protein kinases (MAPKs) family (p38, ERK and JNK) and CA II expression by western blot techniques. AZ action on CA hydratase activity was also measured. Furthermore, Hypoxic inductible factor 1 alpha (HIF-1α) and erythropoietin (Epo) transcripts were determined by real time qRT- PCR.
Results: Our results showed that AZ administration protects efficiently steatotic liver against cold IRI. AZ protection was associated with better function, decreased vascular resistance and activation of eNOS. This was consistent with an effective MAPKs inactivation (p38; ERK and JNK). Interestingly, AZ induced CA II upregulation while decreased CAs hydratase activity. Finally, no changes in HIF-1α and its target Epo mRNA levels were found.
Conclusion: Data reported here demonstrated that AZ is a suitable pharmacological strategy for preserving fatty liver grafts against cold ischemia and reperfusion.

BO386*

A NEW COMPREHENSIVE SCORING SYSTEM IS AN ACCURATE AND ROBUST TOOL FOR HISTOLOGICAL ASSESSMENT OF RAT KIDNEY IRI

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Introduction: Comprehensive documentation of the complex features of kidney IRI is important. The widely adopted "gold standard" Jablonski scoring system for IRI provides a limited score based solely on documentation of the degree of necrosis within tubular cells. We have designed a simple new histology scoring system that accounts for the degree of tissue damage to selected cellular renal components. The aim of this study was to evaluate this new scoring system in an analysis of changes to endothelial, tubular, tubulo-interstitial, and glomerular renal components in rat models of acute IRI.
Methods: Kidney tissue was retrieved at 48 h following surgery on 21 adult male Lewis rats: left unilateral IRI (45-min left renal pedicle cross-clamping) ($n = 5$); left unilateral sham ($n = 5$); bilateral IRI (45-min bilateral renal pedicle cross-clamping) ($n = 9$); and bilateral sham ($n = 8$). Paraffin sections were examined under H&E staining. RNA extraction and RT-qPCR analysis was performed for acute kidney injury (AKI) markers. Serum creatinine was measured before and at 48 h for the bilateral model rats.
Results: 45 minutes of IRI caused marked histological damage characterized by acute tubular necrosis, endothelial cell disruption/loss, tubulo-interstitial damage (inflammation/cast formation), and glomerular capsule thickening. Univariate logistic regression analyses showed that tubular, endothelial, glomerular and tubulo-interstitial damage scores were independently associated with serum creatinine at 48 h. A composite score was calculated from these data. The individual component and composite histology scores correlated significantly with serum creatinine, expression of NGAL and KIM-1, and Jablonski score.
Conclusions: The score derived from our new comprehensive histology scoring system was highly predictive of rat kidney function and structural damage. This system appears reliable, sensitive and valid in assessing the degree of damage in kidney IRI.

BO387* EX VIVO KIDNEY GRAFT PRESERVATION IN A SOLUTION SATURATED WITH ARGON IMPROVES FUNCTION RECOVERY AND SURVIVAL IN PIG

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Aims: The use of noble gases displays promising medical applications. Easy to produce and to use, argon has been shown by our group to have organoprotective capacity in a rat model of kidney transplantation. Here, we further developed this approach using the cold-storage solution Celsior® saturated with 100% of argon at atmospheric pressure (Argon-Celsior) in a clinically relevant pig model of kidney autotransplantation. Celsior saturated with atmospheric air (Air-Celsior) served as control.
Methods: The left kidney was removed and Air-Celsior or Argon-Celsior was used at 4°C to flush and store the transplant for 30 h, a condition that induced in pig significant ischemia-reperfusion injury as shown in preliminary experiments using Air-Celsior. Heterotopic autotransplantation and contralateral nephrectomy were performed. Renal function parameters were monitored for 21 days. Survival and histological characteristics were addressed.
Results: Argon-Celsior versus Air-Celsior: (i) improved graft function recovery as monitored using creatinine clearance, fraction of excreted sodium, and tubulopathy duration; (ii) enabled diuresis recovery 2–3 days earlier; (iii) improved survival (7/8 vs. 3/8); (iv) preserved histological structures as explored by monitoring fibrosis, tubular lesions and inflammation. In strong contrast, the use of another noble gas, xenon instead of argon, was strongly detrimental, no animal surviving at day 8. These data indicate that the effect of argon is not one attributable to noble gases as a group and is specific only to argon.
Conclusions: Together, these data indicate that saturation of a preservation solution with argon improves function recovery, and hence ex vivo preservation of the transplant during cold-storage.

BO388 APOPTOSIS AND NECROSIS MARKERS IN BLOOD IMMEDIATELY AFTER REPERFUSION PREDICT OUTCOME IN HUMAN LUNG TRANSPLANTATION

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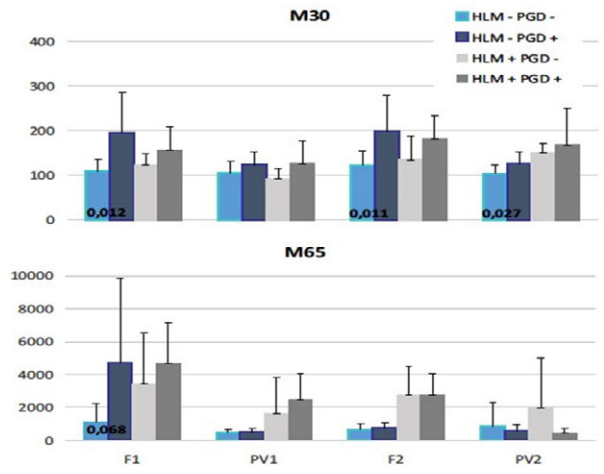
Primary graft dysfunction (PGD) affects lung graft function after transplantation. One of the causes of PGD is ischemia-reperfusion injury accompanied by apoptosis and/or necrosis. The significance of apoptosis and necrosis in PGD is unclear especially after circulatory death (DCD) donation.

This study investigated apoptosis and necrosis in blood after bilateral transplantation (BLTx) of 16 DCD (donation after circulatory death) and 22 DBD (donation after brain death) lungs. Blood samples after reperfusion were analysed using an ELISA kit M30 for apoptosis and M65 for apoptosis and necrosis. Post-transplant PGD was scored (ISHLT grading system).

Overall 23 patients developed PGD (I-III), 17 being persistent at 72 h. PGD after BLTx, 16 with and 22 without heart-lung machine (HLM+/-), was predicted by significant higher M30 levels in the de-airing flushout (F) of the first implanted lung F1 compared to no PGD (177 ± 77, (mean±SD) vs. 112 ± 29, $p = 0.0004$), the second implanted lung F2 (193 ± 68 vs. 68 ± 57,$p = 0.005$) and significant higher M65 levels in F1 samples (4696 ± 4414 vs. 2152 ± 597, $p = 0.030$). Importantly, focusing on the 22 HLM-cases PGD was only predicted by higher M30 levels, see figure.

This study shows that the apoptosis en necrosis markers M30 and M65 in blood immediately after reperfusion are predictive for PGD. Without HLM only M30 predicted PGD.



The bar graphs represent the mean+standard deviation for heart lung machine (HLM+) and no HLM (HLM-) presenting PGD (+) or no PGD (-). PV1 and PV2 represent pulmonary vein samples, 30 min after flushout (F1,F2). p-values; differences between groups.

BO389 BRONCHOALVEOLAR LAVAGE FLUID (BALF) ANALYSIS WITH HIGH RESOLUTION NMR SPECTROSCOPY IN A PRECLINICAL LUNG ALLOTRANSPLANTATION

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Background: Evaluation of preservation protocols for organ transplantation is of primary importance regarding donor pool heterogeneity. We previously present NMR metabolomic analysis of preservation solution in the case of kidney. In the same manner, we propose a NMR analysis of bronchoalveolar lavage fluid (BALF) after an ischemia reperfusion sequence.
Methods: Bronchoalveolar lavage fluid (BALF) was collected after 5 h of reperfusion; explantation of the graft and an upper lobectomy was performed. Washing was done directly by instillation of 40 cc of physiological saline in the left upper bronchus. Samples were centrifuged and supernatant kept at −80°C until high resolution NMR acquisition on an Avance 500SB Spectrometer (Bruker) equipped with a 5 mm broadband inverse probe. Three groups of lung preservation protocol were studied: static preservation with Perfadex solution alone, static preservation with Perfadex solution with addition of an oxygen carrier and sham operated lung ($N = 5$ in each group).
Results: In the control lung, the BALF appears to be clean and we found only few metabolites in low concentrations as lactate. We also found in the NMR spectra metabolites from cell release as choline compounds. BALF from lungs preserved with Perfadex alone showed spectra more complex with higher concentrations of lactate, addition of some metabolites aminoacids (valine, alanine) or sugar body (probably dextran-40 from prefadex solution). The last group with lung preserved with perfadex solution with addition of an oxygen carrier showed intermediate NMR profiles with intermediate concentration. The oxygen carrier seems to have a real impact on BALF composition.
Conclusion: We proposed descriptive and preliminary results on BALF analysis by NMR with a comparison of two lung preservation protocols versus healthy lung.

BO390* FATE AND ROLE OF THE CYTOSKELETTON DURING COLD ISCHEMIA

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Background: Ischemia reperfusion lesions are an unavoidable consequence of organ transplantation. Researching new therapeutics against these require the definition of early mechanisms. The cytoskeleton is composed of 3 types of filaments: microfilaments, intermediate filaments and microtubules. We aimed to characterize the influence of preservation conditions on their phenotype.
Methods: In an *in vitro* model using primary human endothelial cells reproducing the conditions of organ preservation, two aspects were explored: 1-function: using pharmaceutical agents to stabilize microfilaments (Jaspakinolide) and microtubules (Taxol), we determined if maintaining the filament structure could decrease cell death; 2-mechanism: to define the determining factor in cytoskeleton alteration, we separated each of the 3 parameters altered during preservation: solution (culture medium versus preservation solution), oxygen (normoxia versus anoxia) and temperature (37°C vs. 4°C).
Results: 1-Intermediary filaments, made of vimentin in these cells, were unaffected. 2-Microfilaments showed radical changes: progressive disappearance of the structure replaced by a disorganized array of nodules. 3-Microtubules almost completely disappeared with time. The results of the first aspect showed that pharmaceutical intervention could indeed preserve fiber structure but did not alter survival. Regarding the second aspect, our study shows that temperature, and not oxygen deprivation or the solution, was the determining factor of the cytoskeleton's loss of integrity observed during preservation.
Conclusion: Our work shows that a more adapted temperature, not necessarily more oxygen, could profoundly improve cytoskeleton organization and thus the cells ability to restore its function after reperfusion. The impact of preservation on the cytoskeleton highlights the importance of this structure for the development of new therapeutics and the definition of biomarkers of graft quality.

005 COMPOSITE TISSUES

BO392 CLINICAL AND IMMUNOLOGICAL UPDATE 15 YEARS AFTER THE FIRST VCA – SUBSEQUENT KIDNEY TRANSPLANTATION AFTER A BILATERAL HAND TRANSPLANTATION

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Introduction: Clinical and immunological follow-up of the Innsbruck hand transplant program with focus on a subsequent kidney transplantation after successful bilateral hand transplantation.
Patients: Between March 2000 and March 2014, five patients received a bilateral hand, a bilateral forearm or a unilateral hand transplantation. All patients received induction therapy with antithymocyte globulin or alemtuzumab, which was followed by tacrolimus, prednisolon, MMF or tacrolimus and MMF maintenance immunosuppression (IS). In patient #5 an acute renal failure occured immediately after the bilateral hand transplantation. To avoid CNI-toxicity, belatacept has been started and we performed a kidney biopsy.
Results: Hand function of the fifth patient correlated well with time after transplant and amputation level. Two rejections episodes occured (Banff grad II and I-II) which could be treated successfully with steroids. The kidney biopsy revealed severe arteriosclerosis without any reasonable chance for recovery of renal function. There were no signs for tacrolimus induced nephrotoxicity. Due to the dependence on dialysis, he was put on the kidney transplant waiting list promptly. The deceased donor kidney transplantation was done in October 2014. He got basiliximab as an induction agent and the maintenance IS with belatacept was continued according to the BENEFIT-protocol. Initial renal function was excellent. Skin histology at current shows no lymphocytic infiltrates. Luminex-screening for DAS has been negative. Radiomorphological studies do not show any signs for luminal narrowing.
Conclusion: Hereinafter we outline the first case of a kidney transplantation in a VCA-case. The overall outcome and the patient satisfication is encouraging.

BO393 DONOR LIMB HARVEST IN HAND AND UPPER EXTREMITY TRANSPLANTATION: TOWARDS A UNIFIED PROTOCOL

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Background: Hand and upper extremity transplantation offers a superior reconstructive solution for select patients lacking a functional upper limb. Essential to the success of these increasingly popular endeavours is the donor limb harvest process. At present, no consensus or guidelines exist for this aspect of the transplantation. Here we describe and provide an illustrative overview of the surgical technique and possible sequence of events that may occur for the donor harvest procedure.
Methods: Medical illustrations and clinical photography were utilised. Leading medical search engines were queried for relevant articles, and their references included to augment the search.
Results: Considerations in donor selection were categorised into practical, limb-specific, and medical and immunological considerations. All donors were cadaveric multi-organ donors after obtaining specialised consent for limb donation. Harvest of the life-preserving solid organs (SO) should always be prioritised and a pre-harvest plan devised. The limb harvest may occur prior to, simultaneous with, or post SO harvest. Harvests in all three time frames were reported, the most common being limb harvest prior to SO recovery. Differences existed in the timing of instillation and choice of preservation fluid. Following transfer to the recipient operating room, tissue-specific preparations guide the back-table dissection. Throughout all aspects of the harvest process, a distinct variability in reporting was noted in the literature.
Conclusion: The described organisation of the possible sequence of events has built a platform for more consistent reporting, research and future guidelines. It is of vital importance that all individuals involved, including the SO harvest teams and donor hospital staff are familiar with this procedure. Ultimately, standardised protocols will facilitate the widespread use of this novel reconstructive modality.

BO394 THE REVERSE PARADIGM OF CHIMERISM INDUCTION: DONOR CONDITIONING WITH BONE MARROW TRANSFER FROM THE RECIPIENT FACILITATES VASCULARIZED COMPOSITE ALLOGRAFT SURVIVAL

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Background: Rodent models confirmed that infusion of donor-derived bone marrow cells (BMC) at the time of vascularized composite allotransplantation (VCA) can induce donor-specific tolerance via establishing mixed hematopoietic chimerism. We propose a new approach for induction of tolerance in VCA via donor conditioning with recipient BMC transfer.
Methods: The ACI donor rats were conditioned with 80 × 106 of PKH26 stained Lewis recipient BMC, 24 or 72 h prior to transplantation of a VCA (vascularized skin allograft). Fifty VCA were performed between ACI donors and Lewis recipients. In groups I and II, donors were preconditioned 24 or 72 h prior to transplantation, respectively and recipients received anti-αβ-TCR and Cyclosporine-A (CsA) for seven days post transplantation. In groups III and IV, donors were preconditioned 24 or 72 h prior to transplantation, respectively and recipients received no immunosuppression. In group V, donors were not preconditioned, and recipients received anti-αβ-TCR/CsA for seven days post transplantation. In group VI, donors were not preconditioned, and recipients received no immunosuppression. Assessment included evaluation of transplant viability and induction of donor-specific chimerism via flow cytometry, immunofluorescence and PCR.
Results: The presence of PKH-26+ Lewis BMC was confirmed in preconditioned donor's blood, BM, lymphoid organs and liver at 24 h and 72 h. Groups III, IV and VI rejected the allografts, at an average of eight, 14 and 10 days. In groups I, II and V, mean survival was 80, 64 and 30 days. In groups I and II, donor specific chimerism in the peripheral blood decreased from 8.8% and 11.4% on day seven to 3.7% and 4.7% respectively when the flaps manifested grade three rejection.
Conclusions: Donor preconditioning is a novel approach, which modifies recipient's responsiveness to donor allograft and extends the allograft survival under short-term immunosuppressive therapy.

BO395 ATYPICAL CHRONIC TRANSPLANT VASCULOPATHY WITHOUT SIGNS OF SKIN REJECTION IN HAND TRANSPLANT RECIPIENT

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We present the case of vasculopathy without any signs of skin rejection. The 27-year-old man received the right hand transplant allograft at the wrist level in 2008. The immunosuppression consisted of: basiliximab, tacrolimus, mycophenolate mofetil and methylprednisolone. The recipient has suffered previously from G1 rejection episode at the early post-operative period. In June 2014 the patient suffered from diffuse erythema of allograft skin, intense oedema and decrease of hand motor function. The biopsy showed no signs of acute or chronic rejection of the skin. The deep biopsy containing three arteries of various caliber revealed proliferation and accumulation of myofibroblast with lymphocytic infiltration in the arterial wall. Mild focal perivascular lymphocytic infiltrates (70% T-cell, 30% B-cell) were also seen. Intimal hyperplasia and medial thickening without duplication of internal elastic lamina was observed. The deep connective tissue presented intense increase of collagen and elastin fibers with its mechanical destruction and vascular compression. C4d staining was negative. The diagnosis of chronic vasculopathy was established. Positive non-donor specific anti-HLA class II antibodies were observed in the recipient serum. The molecular studies of gene expression in peripheral blood mononuclear cells (*CD4*, *CD8*, CTLA4, *GZMB*, *FOXP3*, *IL10*, *IL4*, *ILR2A*, *NOTCH*, *PDCD1*, *PRF1*, *TGFB*, *TNFA*) as well as T-cell subsets did not differ from other four hand-transplant recipients that we have also studied at the same time. The patient was treated with steroids, plasmaphereses and IVIG together with increased tacrolimus and mycophenolate mofetil doses, and partial improvement was observed.
Conclusion: Chronic transplant vasculopathy may occur without the presence of skin rejection in the hand allograft. Also no serum, gene or immune cell

hallmark of transplant vasculopathy may be noted. Though, the deep graft biopsy should be a part of routine care of VCA recipiens.

BO396* THE INTERNATIONAL REGISTRY ON HAND AND COMPOSITE TISSUE ALLOTRANSPLANTATION (IRHCTT)

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The IRHCTT includes upper extremity and face allotransplantations (HT and FT). Since September 1998 77 HT, 25 unilateral and 26 bilateral transplants, for a total of 51 patients have been reported. In the majority of cases the level of amputation was distal, but there were also 7 arm transplantations. Since November 2005 28 cases of FT have been reported. In the majority of cases the deficit included cheek, nose, chin, lips and perioral area. In HT and FT the immunosuppressive therapy included tacrolimus, mycophenolate mofetil, sirolimus and steroids; polyclonal or monoclonal antibodies were used for induction. Five patients died: 1 case of simultaneous face and bilateral hand transplantation, 1 of bilateral arm transplantation, 1 of bilateral hand transplantation and 2 cases of FT. Eight HT patients have lost their grafts: in 4 cases it occurred in the first period after transplantation (poor vascularization or infectious complications) and in other 4 during the follow-up (chronic rejection/graft vasculopathy). One face graft was removed for unknown cause. Seventy-six percent of recipients experienced at least one episode of acute rejection within the first post-transplant year. Five cases of chronic rejection in HT and one in FT have been reported. Complications included, as in solid organ transplantation, opportunistic infections, metabolic complications and malignancies. Hand-grafted patients developed protective sensibility, 90% of them tactile sensibility and 82.3% developed also a partial discriminative sensibility Motor recovery enabling patients to perform most daily activities. Face-grafted patients improved their aesthetic aspect and they were able to perform some activities such as eating, drinking and speaking which were impossible before FT.HT and FT are successful procedures, however careful evaluation of patients before and after transplantation are indispensable.

BO397 ABDOMINAL WALL TRANSPLANTATION: A SENTINEL MARKER FOR REJECTION

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[1]Charité – Universitaetsmedizin Berlin; [2]Oxford University

Abdominal wall transplantation (AWT) has revolutionized difficult abdominal closure after intestinal transplantation (ITX). More importantly, the skin of the AWT may serve as an immunological tool that is useful in the differential diagnosis of bowel dysfunction after transplantation. Between 2012 and 2014, 14 patients (mean age 38.5 $\pm$ 13.4 years) received AWT from the same donor to complement ITX at the Oxford Transplant Centre. Two doses of alemtuzumab were used for induction therapy (30 mg, 6 and 24 after reperfusion) tacrolimus (trough levels 8–12 ng/ml) was used for maintenance immunosuppression. Four recipients had biopsy proven rejection of the skin on their AWT. These patients did not demonstrate concurrent intestinal graft rejection. In contrast, in one patient with bowel dysfunction (fever,diarrhoea), the skin of the AWT remained normal. Intestinal histology was reported as CMV disease. The skin component of the AWT may serve as a sentinel marker for immunological activity in the host. This is a vital tool for timely prevention of intestinal graft rejection and more importantly the avoidance of overimmunosuppression in cases where bowel dysfunction manifests without the skin component being affected.

BO398 RAT FORELIMB ALLOTRANSPLANTATION: A NOVEL MICROSURGICAL MODEL FOR OPTIMIZED FUNCTIONAL ASSESSMENT AFTER RECONSTRUCTIVE TRANSPLANTATION

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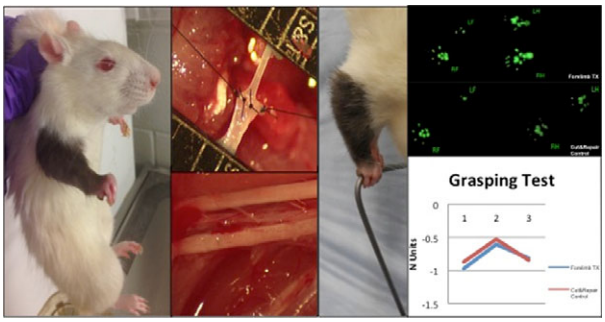
Johns Hopkins University

Background: Functional outcomes following vascularized composite allotransplantation (VCA) have been promising, but there is still much room for improvement. Studies to investigate strategies to overcome this obstacle are limited by the lack of a functional VCA animal model. The rat hindlimb transplant model can be used for histologic and electrophysiologic measures of nerve regeneration but does not allow for reliable assessment of behavioral functional recovery. To address this problem, we developed a novel forelimb transplant model in which functional recovery is tested by measuring progressive return of grip-strength within the transplanted forelimb.
Methods: Rat orthotopic forelimb allotransplantation (Brown Norway to Lewis) is performed at mid-humerus level, with end-to-end cuff anastomosis of brachial artery and vein. Median and radial nerves are approximated in the experimental group to innervate extrinsic flexor and extensor muscles, respectively. A well-established cut and repair model serves as control group (N = 8 per group).
Results: After an initial learning curve, forelimb transplantation can be performed with consistent success (operative time 180–220 min). Long-term graft survival (120 days) was achieved with immunosuppressive treatment (cyclosporine A 10 mg/kg/day). When dangled by the tail with the native arm bound, experimental (innervated) animals reflexively use the transplanted forelimb to grasp a bar, with progressive improvement in grip strength observed beginning at 3 weeks. After 10 weeks, Catwalk and grasping results are comparable to the cut and repair control group.
Conclusion: Rat forelimb transplantation may represent the first VCA model that allows for reliable and reproducible measurement of functional recovery. Statistical analysis of grip strength data will elucidate the degree of variability at each time-point and the degree of improvement from week to week as compared to control group.



BO399 TOLERANCE INDUCTION TO VASCULARIZED COMPOSITE ALLOGRAFTS BY COSTIMULATION BLOCKADE

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Reconstructive transplantation is an emerging era in transplant medicine and a valid therapeutic option after devastating tissue loss. While costimulation blockade (CTLA4Ig) has shown efficacy in preventing rejection of solid organ transplants, its efficacy in VCA remains poorly explored. We investigated the immunoregulatory potential of CTLA4Ig in a novel murine model of hindlimb transplantation. Fully MHC-mismatched allogeneic, orthotopic hindlimb transplants were performed from Balb/c to C57BL/6 mice. Recipient groups received (1)no treatment; (2)CTLA4 Ig on postoperative days (POD)0, 2, 4, 6; (3) CTLA4Ig plus anti-CD154mAb (CoB) on POD0, 2, 4, 6; or (4)non-myeloablative whole body irradiation (WBI) on POD-1 combined with CoB. Secondary skin grafts were performed in longterm survivors. Mixed chimerism, clonal deletion of alloreactive Tcells, intracellular cytokine production, and Thelper phenotypes were analyzed by flow cytometry. CoB recipients showed increased survival compared to untreated and CTLA4Ig only treated groups (MST 82 vs. 8 days,16.5d; p210d; $p < 0.01$). Mixed chimerism induced by donor derived bone marrow components was detected in the CoB treated group, and was detected at even higher levels in WBI+CoB treated recipients (donor CD11b+; 5.5 $\pm$ 3.1 vs. 13 $\pm$ 8, $p < 0.01$). Decreased vβ11 + and vβ5 + CD4 + T cells were detected in both groups treated with either CoB or WBI+CoB, suggesting central thymic deletion of donor reactive Tcells. Donor specific tolerance was indicated in longterm survivors in the WBI+CoB treated group by acceptance of donor matched skin grafts and acute rejection of third party skin. In longterm survivors treated with WBI+CoB, decreased IFN-gamma production from CD4 + T cells was detected. Increased graft-infiltrating Tregs were detected on POD50, however, the decreasing trend suggests a possible shift from central to peripheral regulatory mechanisms. CoB prevents VCA rejection and establishes donor specific tolerance induced by intrinsic BM in the VCA.

BO400

IMMUNE MONITORING OF VASCULARIZED COMPOSITE ALLOGRAFTS USING NON-INVASIVE IMAGING MODALITIES IN A TRANSLATIONAL LARGE ANIMAL MODEL

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Background: To evaluate imaging modalities such as 3CCD and infrared (IR) imaging as a means of non-invasive monitoring of graft acceptance and rejection in the setting of vascularized composite allotransplantation.
Methods: Heterotopic hind limb transplantation in swine was performed across a full SLA-mismatched barrier. Animals were assigned to groups A) untreated control, B) standard immunosuppression with Tacrolimus and C) pulsed immunosuppression. Images of the graft and recipient were taken with 3CCD and IR cameras on the day of transplantation as well as on postoperative days (POD) 2–6, 8, 10, 30 and 60. Additionally, invasive sampling of full thickness graft and recipient skin for histopathology and Raman spectroscopic analysis was performed.
Results: Untreated controls rejected the graft as defined by epidermolysis of the skin component within 5 days post transplantation ($n = 3$). Animals receiving standard immunosuppression maintained their allograft without any clinical signs of rejection ($n = 1$). Both 3CCD and IR imaging show no significant changes from baseline values indicating vital grafts at POD2 in both treated and untreated animals. However, analysis of data collected on POD4 reveals a large decrease (12–32%) in 3CCD intensity values compared to POD 2 intra-individually as well as across treatment groups. Host tissue surrounding the graft and the underlying donor tissue, demonstrates an increase (24–43%) in infrared intensity values compared to both the graft and adjacent host tissue. Raman spectra signify molecular changes in the graft tissue as early as POD2, evidenced by loss of lipid content and increased collagen content. Lipid loss in graft tissue was not as evident in animals with full immunosuppression.
Conclusion: Preliminary data obtained by this study shows that non-invasive imaging modalities detect subtle physical property changes in tissue homeostasis during an ongoing immune response after vascularized composite allotransplantation.

011 HEART

BO401* VARIABILITY IN HEALTH CARE WORKERS' PRACTICE PATTERNS AND HEART TRANSPLANT PATIENTS' MEDICATION ADHERENCE ACROSS 11 COUNTRIES – THE BRIGHT STUDY

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Very limited information is available on healthcare workers' (HCW) practice patterns in view of medication adherence advice given to heart transplant (HTx) patients. Moreover, variability in HTx patients' immunosuppressive non-adherence (INA) across different healthcare systems has not been examined. Aims: To assess HCW's practice patterns in view of medication adherence advice given to HTx patients and variability in HTx patients' INA internationally.
Method: Secondary data analysis of the BRIGHT study, an international, cross-sectional study in 37 HTx centers and 11 countries (Australia, Belgium, Brazil, Canada, France, Germany, Italy, Spain, Switzerland, the UK, the US). 1010 adult HTx patients between 1 and 5 year post-Tx were included. Practice patterns in view of HCW's medication adherence advice given to HTx patient's was assessed by asking patients if they had received this type of advice in the past year. INA was assessed using the BAASIS, a self-report instrument assessing different dimensions of medication taking. Data were analyzed using descriptive statistics.
Results: Overall, 93.2% of patients reported having received advice concerning the intake of their immunosuppressants (range: 85.7% Australia – 100% UK, Brazil, Switzerland). Across all countries, the mean INA levels were: taking INA: 16.1% (range: 4.9% Italy – 25.4% Canada); timing INA: 27.3% (range: 13% UK – 42.9% Australia); drug holidays 1.4% (range: 0% France, Germany, Italy, Spain – 6.3% Brazil); dose reduction: 1.3% (range: 0% Australia, Brazil, Germany, UK – 4.3% Switzerland); overall INA: 35.4% (range: 21.7% UK – 57.1% Australia).
Conclusion: Variability in practice patterns of HCW's in view of medication adherence advice was observed indicating that a proportion of patients had not received advice on medication adherence in the past year. The observed variability in HTx patient's INA across countries suggests that healthcare system factors play a role in explaining INA among HTX patient

BO402* COST-RELATED NON-ADHERENCE AND ITS RELATIONSHIP TO MEDICATION NON-ADHERENCE AMONG ADULT TRANSPLANT RECIPIENTS IN ELEVEN COUNTRIES – A MULTICENTER CROSS-SECTIONAL STUDY

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Problem: Cost-related non-adherence (CRNA), i.e., not taking medications as prescribed due to difficulties in patients' ability to pay for them, is an important barrier to medication adherence and is understudied in solid organ transplantation. We aimed to assess the prevalence of CRNA in heart transplant recipients (HTx) internationally, and to evaluate correlates of CRNA.
Methods: Using data from the cross-sectional BRIGHT study, which used multistage sampling (37 HTx centers in 11 countries; 1701 HTx patients), we assessed CRNA with 3 questions (i.e. prescription due to costs, drug holidays due to costs and skipping doses due to costs)defined as CRNA. Theory based CRNA related correlates explored were: age, gender, marital status, ethnicity, education level, insurance coverage, monthly out-of-pocket expenditures for immunosuppressive medications (IS), perceived financial burden, barriers to the intake of IS, belief in benefits of IS, and cost-related self-efficacy. Descriptive analysis was followed with logistic regression using generalized estimation equations.
Results: The overall prevalence of CRNA was 2.8% (range = 0%: UK – 7.1%: France and Australia). Significant correlates of CRNA were being single versus being married/living together (OR = 3.30; 95% CI 1.73–6.31), African American versus white (OR = 3.69; 95% CI 1.93–7.08), lack of medication insurance coverage (OR = 1.98; 95% CI 1.02–3.86), higher monthly out-of-pocket costs (OR = 1.46; 95% CI 1.13–1.90), perception of not having enough money to pay for the IS (OR = 2.22; 95% CI 1.39–3.70), more barriers to IS (OR = 2.21; 95% CI 1.32–3.71). A protective factor was cost-related self-efficacy (OR = 0.51; 95% CI 0.38–0.68).
Conclusion: HTx CNRA varied among countries yet overall was lower than CRNA levels reported in the literature for other chronic medication regimens (i.e., 4%: UK- 37%: US). Identified correlates of CRNA in HTx can guide the identification of patients at risk for CRNA and intervention development to reduce CRNA.

BO403 VARIABILITY IN PRACTICE PATTERNS REGARDING CHRONIC ILLNESS MANAGEMENT AMONG HEART TRANSPLANT CENTERS – PRELIMINARY DATA FROM THE INTERNATIONAL BRIGHT STUDY

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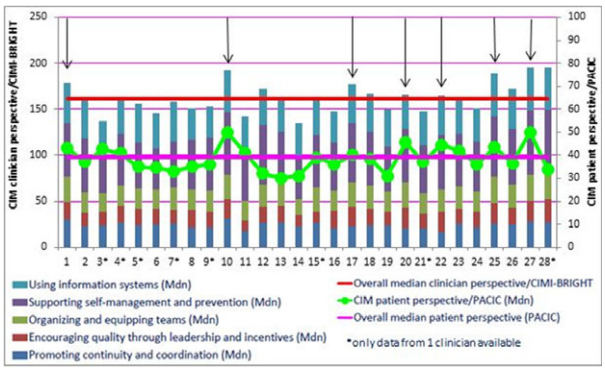
Background: Chronic illness management (CIM) has shown promising results in improving outcomes in chronically ill patients. Limited information exists on the level and variability of CIM implemented in heart transplant (HTx) centers. This study therefore aimed to explore CIM from the patients' and health care professionals' (HCP) perspective in HTx centers.
Method: This was a secondary data analysis of the BRIGHT study, a multi-center, cross sectional study in 37 HTx centers, 11 countries and 4 continents. CIM was assessed through (1) HCP report by the CIMI BRIGHT instrument (55 items, 5 dimensions, range total score: 28 to 220) and (2) patient report using the short version of the Patient Assessment of Chronic Illness Care (PACIC) questionnaire (11 items, range total score: 11 to 55). Data were aggregated at center level. Descriptive statistics were calculated as appropriate. Congruency in CIM between patients and HCP was calculated using Pearsons' correlation.
Results: Preliminary findings from 82 HCP and 1034 patients belonging to 24 centers showed variability in CIM between centers (Intra Class Coefficient = 0). Overall median CIMI BRIGHT score was 161 and the overall median PACIC score was 39 (Figure 1). From all participating centers 7 were above the average. Correlations between patient and HCP perspective were: r = 0.16 (promoting continuity & coordination), 0.46 (supporting self-management & prevention), 0.37 (encouraging quality through leadership & incentive), 0.35 (using information systems) and 0.32 (organization & equipping teams).
Conclusion: We observed variability of CIM among HTx centers with most variability explained at center level, indicating that CIM practice patterns differ among centers. These data provide a basis to identify areas for improvement in CIM. Moreover, positive deviants can be studied qualitatively to learn about best practice patterns concerning CIM to guide centers in improving CIM approaches.



BO404 BINDING OF ATGS TO ENDOTHELIAL CELLS UNDER *IN VIVO* CONDITIONS

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Background: Polyclonal antithymocyte globulins (ATGs) are immunosuppressive drugs widely used in induction of immunosuppression and treatment of acute rejection after solid organ transplantation. We have previously demonstrated that ATG bind to endothelial cells *in vitro*, and are able to modulate ECs. The aim of this study was to investigate the binding of ATGs to endothelial cells under *in vivo* conditions.
Material and Methods: Muscle biopsies from extremities of cynomolgus monkeys were obtained after ischemia/reperfusion at 4 °C. ATGs (1.5 mg/kg) were added to the blood 30 min prior to the reperfusion. Biopsies ($n = 6$) of patients treated with ATG (1.5 to 2.5 mg/kg) as induction therapy before heart

transplantation were also analyzed 6 h and 7 days after induction. Binding of ATG to ECs was analyzed with an anti-rabbit IgG Antibody by means of immunohistochemistry.
Results: Binding of ATGs to endothelial cells could be demonstrated *in vivo* in our animal experiments, 4 h after reperfusion, as well as in the clinical biopsies 6 h after induction of immunosuppression in heart transplant patients, showing a preferred localisation in post-capillary veins. No expression of ATG on the endothelial surface could be observed after seven days, suggesting that ATGs may be washed out from the endothelial surface time dependently.
Conclusion: Our results confirm that ATGs are able to bind to endothelial cells, supporting preconditioning strategies with ATG in solid organ transplantation, as a down-regulation of adhesion molecules by ATG may decrease graft cell infiltration and modulate the endothelial activity.

BO405 ONE-SINGLE DOSE COMPARED TO TWO-DOSE BASILIXIMAB INDUCTION THERAPY IN HEART TRANSPLANTATION: IMMUNE MONITORING AND CLINICAL OUTCOME

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Background: The impact of induction on long-term survival in heart transplantation (HT) is still unclear. Attempts to avoid or reduce dose of induction therapy could be desirable in some cases. On the other hand, reduction in anticalcineurin through levels or delay in the initiation due to renal failure and other settings could be indicated in other cases.
Methods: A comparative analysis between the use of the recommended two doses of 20 mg (2D, $n = 9$) of anti-IL2R-alpha (Basiliximab) versus a single dose (1D, $n = 13$) in selected patients was performed. We analysed lymphocyte reconstitution, rejection, infection and serum cytotoxic antibodies during the first 3 months after transplantation (asessment points: pre-HT, day [d] 7, d15, d30 and d90). Maintenance immunosuppression included steroids, tacrolimus and mycophenolate. Percentages and total counts of lymphocyte subsets and CD4 + CD25 + T-cells were studied by flow-cytometry. Mann-Whitney or Student's-T test were used as indicated.
Results: Mean age was 56 ± 15, 22 patients, 16 men. In both groups a significant decrease of CD4 + CD25 + cells was observed as compared with pre-transplant values. Non significant differences between groups were found in CD4 + CD25 + T cells at all assessment points. Absolute TCD4 + were significantly lower at d7 in the 2D group (161 ± 132 vs. 388 ± 182, $p = 0.016$). Mean number of infections was higher in 2D group (2 vs. 0.6, $p = 0.022$). Delay to the first dose of tacrolimus was greater in 2D group (10 ± 3 vs. 5 ± 3, $p = 0.002$) and creatinine levels were normal at d30 (1.09 ± 0.19 vs. 0.68 ± 0.23 mg/dL). None clinical rejection episodes occurred, biopsies ($n = 120$) disclosed ISHLT rejection grades lower than 1R. Low titer DSA were observed in 1 patient of each group until d90.
Conclusion: In a short-term follow-up study of a single cohort, one-dose of Basiliximab seems to be similar in terms of immunemodulation of CD25, rejection and anti-HLA antibody production compared to a conventional 2-dose regimen.

BO406 RIGHT VENTRICULAR DYSFUNCTION IN BRAIN DEATH: EFFECT OF CORTICOSTEROIDS

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Introduction: Brain death triggers sympathetic storm with a torrent of circulatory catecholamines. Pulmonary edema and ventricular dysfunction can be achieved in return. We developed a model of brain death in pigs and studied right ventricular (RV) function with or without corticosteroids therapy. Heme oxygenase-1 (HO1) is an inflammatory modulator and may play a role in right ventricular dysfunction pathobiology.
Methods & Results: Sixteen pigs (+/- 45 Kg) were randomized to placebo ($n = 9$) or to corticosteroids ($n = 7$) 1.5 mg/kg before brain death (BD). BD was induced by slow intracranial blood (250 cc) infusion. Four hours after BD declaration, the animals underwent a hemodynamic evaluation followed by cardiac tissue sampling for real-time quantitative PCR for HO-1. A control group ($n = 9$) was also studied. Brain death increased cardiac frequency (CF), pulmonary pressure (PAP), pulmonary vascular resistance (PVR), capillary pressure (Pcap) and total RV working (Wtot). Right ventricular end-systolic elastance (Ees) increased but not in proportion to pulmonary arterial elastance (Ea) so that Ees/Ea ratio collapsed. Systemic arterial pressure was decreased while occluded pulmonary arterial pressure did not change. BD was associated with a decrease in RV HO-1 gene expression. Corticosteroids therapy totally prevented changes in CF, PAP, PVR, Pcap, Wtot and Ees/Ea. Corticosteroids therapy was associated with an increased RV HO-1 gene expression beyond control animals.
Conclusions: BD is responsible for RV dysfunction and HO-1 gene expression down regulation. Corticosteroids would maintain the RV-arterial coupling and increased gene expression of the inflammatory modulator HO-1.

BO407 IMMUNOGUIDED MODULATION OF HYPOGAMMAGLOBULINEMIA AS A RISK FACTOR OF INFECTION IN HEART RECIPIENTS. RESULTS OF A CLINICAL TRIAL

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Background: Post heart transplant IgG hypogammaglobulinemia (HGG) is a risk factor for severe infections that can be modulated. In a clinical trial we evaluated the efficacy and safety of intravenous immunoglobulin (IVIG) for prevention of severe infection in heart recipients with post-transplant HGG.
Methods: 12 adult heart recipients who developed HGG (IgG<500 mg/dL) were included in this phase-II, open-label pilot study (EudraCT 2009-011165-85, Recruitment: February 2011 to April 2014). HGG was detected during a screening phase at days 7, 14, 30, 60 and 90 after transplantation. Patients without exclusion criteria received IVIG [Flebogamma 5%, Grifols, Spain] 2 doses of 200 mg/kg (day 0 and day 14 of the trial) followed by up to 5 additional doses of 300 mg/kg (days 30, 60, 90, 120 and 150) if IgG was below 750 mg/dL in samples obtained in previous visits. Primary end-point: Development of severe infections during the first 6 months. Data were matched with 13 heart recipients with post-transplant HGG that were not included in the clinical trial during the same study period.
Results: IgG and specific antibody reconstitution was observed in IVIG-group. Severe infection was detected in 3 of 12 IVIG-treated recipients and in 10 of 13 controls (2-sided Fisher's exact test, $p = 0.017$). Cytomegalovirus infection that required antiviral treatment developed in 2 recipients with IVIG versus in 8 non-IVIG recipients ($p = 0.041$). A lower incidence of severe bacterial infections was observed in IVIG-group (25 vs. 69%, $p = 0.047$). Readmission or prolongued hospitalization due to infection was more frequent in non-IVIG group (64 vs. 11.1%, $p = 0.028$). No moderate or severe IVIG-related side effects occurred.
Conclusion: The data of this pilot study demonstrate that prophylactic use of IVIG replacement therapy guided by immunemonitoring can modulate IgG HGG, is safe, and decreases the incidence of severe infections in heart transplant recipients with HGG.

BO408 EFFICACY AND TOLERABILITY OF STRATEGIES TO REDUCE CYTOMEGALOVIRUS INFECTION ONSET: INSIGHTS FROM THE RANDOMIZED STUDY PROTECT

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Introduction: Cytomegalovirus (CMV) is the most common cause of infection during the first year after heart transplantation (HT). It may be prevented by the use of antiviral drugs in a prophylaxis (PRO) or preemptive (PRE) approach. The balance between toxicity and efficacy of these two approaches in HT is still debated. In addition the interplay of anti-CMV strategy with immunosuppressive regimen and specific anti-CMV immunity is unknown.
Methods: By a 2 × 2 factorial design, CMV seropositive HT recipients were randomized to receive 3 months of valganciclovir PRO or a PRE based approach, and to receive mycophenolate (MMF) or everolimus (EVE) on top of a cyclosporine-based therapy. All were monitored for CMV infection by whole blood PCR and CMV-immunity reconstitution by elispot assay.
Results: 48 patients were randomized: 22 to PRE vs. 26 to PRO, and 25 to EVE vs. 23 to MMF. Drug toxicity represented a relevant issue in the study: 7 (28%) patients discontinued EVE and 15 (57%) did not completed the 3-months period of PRO for adverse events. Regardless the high rate of discontinuation, after adjusting for donor serology, intention to treat with PRO and EVE were associated with reduced risk for CMV reactivation ($p < 0.05$). Of note, EVE discontinuation and lack of PRO completion were associated with increased risk for CMV infection. Recovery of CMV immunity at month 1 by Elispot analysis allowed stratifying the risk for CMV infection: patients with lack of immunity were at higher risk of infection, and most likely to benefit from PRO or EVE ($p < 0.01$).
Conclusions: Although EVE and PRO effectively reduce the risk for CMV reactivation, both strategies showed lower tolerability than MMF and PRE,

exposing patients who discontinue to higher risk of events. Analysis of CMV immunity recovery may provide guidance in customizing therapeutic strategies, by identifying patients likely to have a favorable risk/benefit ratio from aggressive anti-CMV strategies.

BO409 BENEFIT OF EVEROLIMUS ON CARDIAC ALLOGRAFT VASCULOPATHY: FURTHER EVIDENCE FROM IMPUTATION ANALYSES FOR MISSING INTRAVASCULAR ULTRASOUND DATA FROM THE A2310 STUDY

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Background: The benefit of everolimus (EVR) on cardiac allograft vasculopathy (CAV) compared to mycophenolate mofetil (MMF) was previously shown in A2310 IVUS sub-study, by assessing the mean change in average maximum intimal thickness (MIT) between baseline and Month 12 (M12). However, only half of the enrolled patients had evaluable intravascular ultrasound (IVUS). Here, we present imputations under statistical and medical perspectives for the missing IVUS data.
Methods: A2310 study (NCT00300274) randomised 721 heart transplant recipients to EVR [(1.5 or 3.0 mg; each dose with reduced cyclosporine-A (CsA)] or MMF 3.0 g + standard CsA. The IVUS population consisted of patients from prospectively selected sites with IVUS capability. The primary IVUS efficacy endpoint was the mean change in average MIT (surrogate marker for CAV) from baseline to M12. Clinical condition precluding performance of IVUS was the primary reason for missing values which were then imputed using three main methods [Table 1A]. Imputation method A was based on missing at random assumption, whereas methods B and C assumed that the missing values were not at random [probability of missing values depending on missing data due to a medical reason (e.g., renal dysfunction, death) as identified by a medical expert].
Results: The mean change in average MIT from baseline to M12 was significantly smaller in the EVR group versus the MMF group regardless of the type of imputations used. The difference in mean MIT change between the two treatment groups was in favor of EVR in the observed cases, and per imputation A, B and C, respectively [Table 1B].
Conclusion: The sensitivity analyses using different imputation methods confirmed the benefit on CAV of EVR compared to MMF corroborating the robustness of the primary results of the A2310 study.

Table 1

(A) Imputation methods for missing IVUS data (Intent-to-Treat IVUS Population)

Imputation method	Type of missing			
	Missing baseline only	Missing M12 only	Missing both baseline and M12	Less than 11 matches in MIT between baseline and M12
A	Multiple imputation (MI) for MIT change	MI for MIT change	MI for MIT change	MI for MIT change
B	MI for MIT change	MI for MIT change	No imputation	No imputation
C	MI for baseline MIT Then calculate MIT change	- Deaths: Impute with worst change of total population - Renal dysfunction: Impute with 25th percentile change -Others: MI for MIT change	- Deaths: Impute with worst change of total population - Renal dysfunction: Impute with 25th percentile change -Others: MI for MIT change	MI for MIT change

(B) Change in Average Maximum Intimal Thickness (mm) from baseline to M12

Imputation	EVR (1.5 mg) N=184		MMF (3.0 g) N=181		Difference (EVR – MMF)		
	n	Mean	n	Mean	Mean	SE	P-value
Observed	88	0.0251	101	0.0700	0.0449	0.0129	0.0003
Method A	184	0.0301	181	0.0565	0.0264	0.0114	0.0228
Method B	125	0.0233	137	0.0668	0.0435	0.0134	0.0016
Method C	184	0.0309	181	0.0781	0.0472	0.0149	0.0018

BO410 HEART TRANSPLANTATION IN 8 PATIENTS WITH SYSTEMIC SCLEROSIS: RESULTS OF A FRENCH NATIONAL REGISTRY

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Objectives: There is no specific treatment for primary cardiac involvement in systemic sclerosis (SSc). Heart transplantation (HTx) has been reported as a treatment option for these patients. Our goal is to analyze the outcome of patients with SSc and primary cardiac involvement requiring HTx.
Methods: We retrospectively reviewed the charts of adult French patients with SSc and a primary cardiac involvement requiring HTx and compared their outcome to the French HTx historical cohort.
Results: A national registry included all the patients transplanted for cardiac involvement in SSc in France: 8 patients: 5 women, 4 diffuse SSc (dcSSc) and 1 overlap. The median age at SSc diagnosis was 33.5 years. The main indications for HTx were refractory heart failure and recurrent ventricular arrhythmia. Time from cardiac dysfunction diagnosis to HTx was 2.75 years and 6/8 patients were transplanted in urgency status. Infection was the main post-surgical complication, but SSc-specific features such as the intestinal pseudo-obstruction and critical extremity ischemia also complicated the intensive care unit stay where 2 patients died. At last follow-up, 5/7 patients had at least one acute cellular rejection and mild cardiac allograft vasculopathy occurred in 3/5 patients. These results are similar to the aged matched population of french patients transplanted during the same period.
Conclusion: HTx is a treatment option in carefully chosen SSc patients with symptomatic primary cardiac involvement with severe dysfunction and/or arrhythmic complications

003 CLINICAL IMMUNOSUPPRESSION & BIOLOGICALS

BO411 USE OF A SINGLE DOSE OF BASILIXIMAB AFTER MAJOR SURGICAL PROCEDURES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Major surgical procedures in transplant recipients may require in the post-operative period adjustments of the immunosuppressive therapy, because of reduced absorption or risk of nephrotoxicity. We evaluated the use of Basiliximab in this setting, in kidney transplant recipients (KTX).
Methods: Twenty KTX received 20 mg IV infusion of Basiliximab pre-op on the morning of the major surgical procedure. In the post-op period all the maintenance immunosuppressive agents were stopped, with the exclusion of steroids, that were administered IV at the same pre-op dose. After 2 weeks the pre-transplant immunosuppression was resumed. End points of the study at 12 month follow-up were: surgical and medical complications, acute rejection episodes, changes in the pre–postop renal function, need for post-op hemodialysis, graft loss and patient survival.
Results: The study population included 20 KTX with a mean follow-up of 69 months (range 7.7–147), on maintenance immunosuppression based on CNIs in combination with mTORi (70%) or MMF. These immunosuppressive agents were stopped on the day of the major surgical procedure (9 CABG, 4 bowel resections, 2 lung resections, 3 large incisional hernia repairs, 1 major head trauma, 1 total bladder resection for neoplasia). At follow-up 3, 6 and 12 months after surgery, no episode of acute rejection, graft loss and death was observed. Mean pre-op and discharge serum creatinine were 1.42 $\pm$ 0.6 and 1.49 $\pm$ 0.7 mg/dl, respectively ($p = 0.743$), pre-op and 12 months post-op MDRD were 68 $\pm$ 9 and 73 $\pm$ 11 ml/min ($p = 0.654$). One patient had pneumonia requiring prolongation of the hospitalization. No CMV viral infections or wound complications requiring surgical treatment were observed.
Conclusion: Our study shows that in KTX on occasion of major surgical procedure the suspension of immunosuppressive therapy for 2 weeks after surgery and the administration of 20 mg of Basiliximab do not compromise renal function and do not increase adverse events.

BO412 MYLIFE: A PROSPECTIVE OBSERVATIONAL STUDY OF PRESCRIBING PRACTICES FOR ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) IN KIDNEY TRANSPLANT (TX) PATIENTS MANAGED UNDER ROUTINE CONDITIONS IN FRANCE

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Background: The recommended initial dose of EC-MPS (1440 mg/day) may be adjusted according to time post-tx and to accommodate concomitant administration of tacrolimus (TAC) versus cyclosporine (CsA) or co-administration of an mTOR inhibitor (mTORi). Real-life prescribing practice for EC-MPS is largely undocumented.
Methods: MyLIFE was a prospective observational study of adult kidney $\pm$ pancreas transplant patients (pts) starting EC-MPS at 33 centers in France. Data were collected for first EC-MPS dose and at month 6 (M6). The primary objective was to describe the initial EC-MPS dose according to concomitant immunosuppressive therapy.
Results: 465 pts were evaluable (176 *de novo*; 289 > M1 post-tx ["maintenance"]). EC-MPS dose was higher in *de novo* versus maintenance pts at first dose and at M6 (both $p < 0.001$). In *de novo*pts, the mean first EC-MPS dose was significantly lower in pts treated with TAC versus CsA ($p = 0.003$); the difference narrowed slightly but remained significant at month 6 ($p = 0.040$) (Table). EC-MPS was initiated as a result of the center standard practice in 95% of de novo pts and intolerance to another therapy in 47% of maintenance pts. By M6, EC-MPS had been discontinued in 47 pts (10%), most frequently due to adverse events ($n = 32$).
Conclusion: EC-MPS dosing is higher in *de novo* versus maintenance kidney transplant pts, commensurate with declining immunosuppressive intensity over time. EC-MPS dosing appears to be adjusted appropriately to reflect concomitant immunosuppression, based on drug-drug interactions between CsA and MPA and the risk of tolerability issues during co-administration of MPA and mTORi.

		Mean (SD) EC-MPS dose (mg/day)	
	n	First dose	Month 6
All *de novo* pts	176	1418 (349)	943 (346)
TAC	155	1389 (339)[a]	922 (338)[b]
CsA	21	1629 (353)[a]	1100 (380)[b]
All pts > 1 month	289	769 (312)	733 (295)
TAC	212	725 (259)[c]	688 (234)[c]
CsA	55	939 (428)[c]	907 (420)[c]
mTORi	22	769 (300)[c]	720 (302)[c]

[a] $p = 0.003$ TAC versus CsA; [b] $p = 0.040$ TAC versus CsA; [c] $p < 0.001$ across groups.

BO413 EVIDENCE FOR A TWO-HIT MECHANISM IN MYCOPHENOLATE-RELATED CHRONIC DIARRHEA AFTER KIDNEY TRANSPLANTATION

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Background: Chronic diarrhea is a frequent problem after kidney transplantation. Since chronic diarrhea is often attributed to mycophenolate toxicity, immunosuppression is switched to a mycophenolate-free regimen. We hypothesized that drug toxicity is not sufficient to induce chronic diarrhea but that a second hit resulting from intestinal infection is required to trigger chronic mycophenolate-related diarrhea.
Methods: In this retrospective study, all patients receiving a kidney transplant between 2000 and 2010 at University Hospital Zurich were screened until July 2014 for chronic diarrhea (i.e. loose stool for > 1 month). Patients with combined organ-transplantation or with confirmed inflammatory bowel disease were excluded. Evidence for infectious triggers at diarrhea onset was assessed by review of medical history, stool microbiology and histology of colon biopsies.
Results: A total of 51 episodes of chronic diarrhea were registered in the whole cohort of 726 patients. Evidence for intestinal infection at diarrhea onset was found in 38 episodes (74.5%). Diarrhea onset showed a seasonal distribution with peaks in April and October/November. Cumulative incidence of chronic diarrhea was homogenously distributed during post-transplant time, with 2.0%, 5.1% and 9.6% at 1, 5 and 10 years, hence there was no peak incidence in the first months of mycophenolate exposure. Switch of immunosuppression to azathioprine was associated with resolution of diarrhea in all episodes. Interestingly, re-introduction of mycophenolate following conversion to azathioprine in 5 episodes was not followed by diarrhea relapse.
Conclusion: These results suggest a two-hit mechanism of chronic diarrhea during therapy with mycophenolate. Mycophenolate alone seems not sufficient to induce chronic diarrhea but rather perpetuates infection triggered diarrhea. Thus, a short switch to a mycophenolate-free regimen might be sufficient to truncate chronic diarrhea if the infection has been cleared.

BO414 IMPACTS OF MYCOPHENOLATE MOFETILE ADDITION TO VERY LOW EXPOSURE EVEROLIMUS AND CALCINEURINE INHIBITOR BASED IMMUNOSUPPRESSION IN DE NOVO KIDNEY TRANSPLANTATION

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Purpose: Prospective randomized study of MMF addition to everolimus (EVR) based immunosuppression was evaluated in clinical outcomes as well as protocol biopsies findings and donor specific antibody (DSA) production.
Methods: Thirty de novo kidney transplant recipients were treated with reduced-exposure cyclosporine (CsA; target C0 100–150 ng/ml for 2 months and consequently reduced 50 ng/ml after 6 months), EVR (EVR-C0 were adjusted 5–8 ng/ml), corticosteroid and basiliximab induction. The recipients were prospectively randomized into two groups at 6 months after transplant, 1) EVR group: continuing CsA and EVR unchanged and 2) EVR+MMF group: CsA and EVR were further reduced to achieve 25–50 ng/ml in CsA-C0 and 3–5 ng/ml in EVR-C0 with addition of MMF starting 1000 mg/day, and adjusted to obtain MPA-AUC0-12 between 30–45 μg•hr/L. The primary endpoints were the effect on eGFR, proteinuria, protocol biopsy findings and DSA production with MMF addition after one year.
Results: With a mean observation period of 21 (12–30) months, patient and graft survival is 100% in both groups (EVR; $n = 15$, EVR+MMF; $n = 15$). EVR-

C0 and CsA-C0 at 1 year after transplant was significantly reduced in EVR+MMF group (3.8 ± 1.9 and 42 ± 17 ng/ml) compared to EVR group (5.7 ± 1.6 ng/ml and 72 ± 37 ng/ml) ($p < 0.05$). Renal function expressed as eGFR was similar 47.7 ± 14.1 in EVR group and 39.7 ± 10.0 in EVR+MMF group. Significant proteinuria, more than 500 mg/day, were observed more in EVR+MMF group (33%) than in EVR group (7%) respectively. One (6.7%) of EVR+MMF group was treated for clinical T cell mediated rejection, but no others revealed clinical or subclinical T cell and antibody mediated rejection on 1 or 12 months protocol biopsies.
Conclusions: MMF addition with further reduction of EVR and CNI did not lead benefit in eGFR, proteinuria, protocol biopsy findings and DSA production. Further evaluation is needed on DSA production with longer term follow-up.

BO415 SAFETY AND EFFICACY OF LOW DOSE AND VERY LOW DOSE EXTENDED-RELEASE TACROLIMUS/MMF IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Recently, once-daily tacrolimus extended-release formulation (TACER) has been accepted in kidney transplantation, however its optimal dosing are not well evaluated. We have validated low dose (LD) and very low dose (VLD) TACER / MMF protocol in de novo kidney transplant recipients.
Patients and Methods: Thirty-eight Living-donor kidney transplant recipients were prospectively randomized into two group, (1) LD group ($n = 19$); targeting tacrolimus area under curve profiles (TAC-AUC) 0–24 by limited sampling strategy 250 ng•hr/ml during the first 1 months and reduced to 200 ng•hr/ml after 3 months. (2) VLD group ($n = 19$); targeting TAC-AUC0-24 200 ng•hr/ml during the first 1 months and reduced to 150 ng•hr/ml after 3 months. All administered in combination with mycophenolate mofetile (MMF), corticosteroid and basiliximab induction. MMF was started with 1250 mg bid and reduced to 750 mg bid at 2 weeks after transplant, and adjusted to achieve MPA-AUC0-12 between 30–60 μg•hr/L. Subclinical rejection and CNI toxicity were evaluated by protocol biopsy after 1 and 12 months.
Results: With a mean observation of 16 months (6–25), patients and graft survival are 100% in both groups. Subclinical or clinical T cell mediated rejection were observed in 0 (0%) in LD group and 1 (5.2%) in VLD group. Incidence of CMV infection was significantly reduced in VLD group (9.1%) compared to LD group (33%) respectively. Mean eGFR were equivalent between the two groups and maintained at 53.6 ± 12.6 ml/min/1.73 m^2 in LD group and 58.6 ± 12.4 ml/min/1.73 m^2 in VLD group at 1 years after transplant. Mean tacrolimus trough concentration at 1 week, 1 month and 1 year after transplant was 7.7 ± 3.0, 5.5 ± 2.4, 4.8 ± 0.8 ng/ml in LD group, and 8.2 ± 3.0, 4.8 ± 1.0, 3.2 ± 0.7 ng/ml in VLD group. Significant difference was observed at 1 year after transplant ($p < 0.05$).
Conclusions: TACER combination with MMF can be safely reduced to very low level without significant increased incidence of rejection.

BO416 A STEADY-STATE PHARMACOKINETIC COMPARISON OF ALL FK-506 FORMULATIONS (ASTCOFF STUDY): AN OPEN LABEL, PROSPECTIVE, RANDOMIZED, TWO ARM, THREE PERIOD CROSSOVER STUDY

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Envarsus® XR (Envarsus in EU, E) is a novel once-daily tacrolimus (tac) formulation with improved bioavailability, lower peak, less peak-to-trough fluctuation, similar safety, and non-inferior efficacy versus twice-daily tac capsules (Prograf®, P). This open label, randomized, crossover study compared the steady state pharmacokinetics (PK) of once-daily E to twice-daily P and once-daily Astagraf XL (Advagraf in the EU, A) in stable renal transplant recipients. Patients were randomized to receive P for one week and then either E or A for one week, followed by the alternate formulation for the following week, using a mg to mg conversion factor of 1:1:0.80 for P:A:E respectively. No dose titrations were allowed. Tac level sampling was conducted over 24 hrs at the end of each 7-day period. Thirty patients comprised the PK per-protocol population (mean age 49 yrs; 57% male; 73% Caucasian). There were no statistically significant Period or Sequence effects. The table includes observed PK parameters that showed significantly higher exposure on a per mg basis, lower intra-day fluctuation and prolonged time (Tmax) to peak concentration (Cmax) for E versus P or A. Conversely, A did not show any differences when compared to twice-daily P in exposure, Cmax, Tmax or intra-day fluctuation in blood levels ($p = NS$). The observed exposure of P was used to normalize exposure for E and A as depicted in the figure and showed lower Cmax and longer Tmax for E but no differences between A and P. Renal function was similar across formulations. Adverse events (AEs) were reported for P (9.7%), A (32.3%), and E (19.4%). No serious AEs. ASTCOFF is the first PK study to compare all three branded formulations. The E PK parameters differed significantly from A and P, while A and P tended to be similar to each other. This also highlights potential clinical benefits from a novel drug delivery system, resulting in the following recommended total daily dose conversions rates: P:A, +8%; P:E, −30%; A:E, −36%.

BO417* AN EASY ALGORITHM TO OPTIMIZE THE EXPOSURE TO TACROLIMUS AND EVEROLIMUS, WHEN USED IN COMBINATION

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The combination of tacrolimus (TAC) and everolimus (EVR) is now used for the treatment of renal transplant recipients (KTx). Preliminary data indicate that this combination may provide benefit without increasing the risk of acute rejection, but may be responsible of nephrotoxicity. The optimal exposure to the two drugs when used in combination is still not known. We evaluate an easy algorithm combining the trough blood levels of TAC and EVR to optimize there exposure.

We retrospectively evaluated the trough blood levels of TAC and EVR, creatinine and eGFR in 64 KTx followed up for 28 ± 38 months (range 3–110 months). We calculated the average sum of the TAC+EVE through blood levels (SUM) in stable KTx with or without signs of acute nephrotoxicity. Renal toxicity (NeTox) was defined as creatinine increase less than 25% from nadir levels, reversible with reduction of one or both drugs.

36 KTx (56%) experienced at least one episode of NeTox, while 28 KTx never showed NeTox (NOTOX). At the time of diagnosis of NeTox creatinine was 2.03 ± 0.83 mg/dl and decreased to 1.67 ± 0.73 mg/dl after reducing the two drugs (RED) ($p < 0.0001$); eGFR was 38 ± 16 ml/min in NeTox and increased to 48 ± 21 ml/min after RED ($p < 0.0001$). In NeTox SUM was 13.2 ± 3.9 ng/ml and after RED 8.2 ± 1.2 ng/ml ($p < 0.0001$). TAC was reduced from 7.3 ± 3.0 to 4.6 ± 0.9 ng/ml ($p < 0.0001$) and EVE was reduced from 5.9 ± 2.0 to 3.6 ± 0.7 ng/ml ($p < 0.0001$). In KTx without any episode of NeTox, eGFR was significantly better than in NeTox after RED (66.7 ± 21 vs. 48.2 ± 21.4 ml/min, $p < 0.001$), while SUM was not significantly different in NOTOX in comparison with NeTox after RED (8.5 ± 0.9 vs. 8.2 ± 1.2 $p = 0.218$).

Our study indicate that patients who experienced nephrotoxicity during the maintenance phase after renal transplantation have a reduced eGFR. Our data suggest that when using the combination of TAC+EVE, keeping the sum of TAC+EVE through blood levels below 10 ng/ml, can significantly reduce the renal toxicity of thi combination.

BO418 EVEROLIMUS, TAC-ER AND MMF DE NOVO RENAL TRANSPLANT RESULTED GOOD GRAFT FUNCTION

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Introduction and Aims: Everolimus (EVR), mTOR-I expect good graft function by avoiding nephrotoxity, and lower incidence of viral infection and carcinogenesis. We started de novo transplant with EVR, Tac-extended release (TER) and MMF with low-dose steroid from 2012. In this study we compared the result of 2 years follow-up of EVR regimen with the previous regimen without EVR.
Methods: We initiated EVR of 1.5 mg/day from 14 days post-transplant and control at the C0 of 5 ng/ml. PSL is gradually reduced to 2.5 mg by POD 30. TER is started with 0.15 mg/Kg and maintained with C0 level of 8 ng/ml until POD 14, then reduced to 5 ng/ml after EVR initiation. MMF is also reduced from 2000 to 1000 mg at same time. Other immunosuppressions were same but TER was maintained at C0 level of 8 ng/ml and MMF was 1500 mg in the regimen without EVR. We evaluated the results between two groups with and without EVR (33 cases) in terms of the graft and patient survival, graft function, incidence of biopsy proven acute rejection (BPAR), and adverse events.
Results: We experienced 25 cases with average follow-up of 16.7 (2.6–31.3) months. Mean age of the recipients was 47.6 years. Three cases were ABO incompatible. Both patient and graft survival were 100%. The average sCr (eGFR) at 3, 6, 9, 12, 18 and 24 months post-transplant were 1.58 (40.1), 1.50 (41.4), 1.61 (37.3), 1.66 (36.9), 1.54 (39.5) and 1.65 (32.7) mg/dl (ml/min/1.73 m) respectively. The graft functions were similar between two groups. Only 1 (4%) BPAR was observed in EVR group (12.1% in without EVR). No CMV infection was encountered in EVR group (69.7% in without EVR). However; some adverse events were noticed; 8 cases had stomatitis (32%), 2 (8%) of each pancytopenia, hyperlipidemia, and proteinuria. Finally we had to discontinue EVR in 9 cases out of 25.

Conclusions: EVR+TER de novo renal transplantation resulted in good graft function, little incidence of rejection and viral infection, but some adverse events require to pay attention.

BO419 EVEROLIMUS-BASED IMMUNOSUPPRESSION IS ASSOCIATED WITH A REDUCED RISK OF NEW-ONSET MALIGNANCIES AFTER LIVER TRANSPLANTATION

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Background and Aim: The inhibitor of the mammalian target of rapamycin (mTOR) everolimus (EVR) has shown anti-proliferative effects in experimental and clinical models. We investigated whether liver transplant (LT) recipients on EVR-based immunosuppression had comparable outcome in terms of the incidence of new-onset post-transplant malignancies (NOPTM) versus patients receiving calcineurin inhibitors (CNI).
Materials and methods: This was a retrospective analysis of a single-center, prospectively collected database. Between January 1996 and December 2013, 1,510 LT procedures were performed on 1437 patients. A total of 243 patients received EVR for reasons other than de novo or recurrent malignancies and were compared against 1182 patients on CNI-based immunosuppression (total data set = 1425 patients). Data were censored until occurrence of NOPTM, death, lost to follow-up or as of November 2014.
Results: At a median follow-up of 1740 days (range 1–6510), a total of 43 NOPTM was observed (3.01%). Two (0.8%) NOPTM were observed in the EVR group (median follow-up 1050 days; range 7–2880) (1 skin cancer, 1 post-transplant lymphoproliferative disease (PTLD)) versus 41 (3.4%) in patients on CNI (median follow-up 3121 days (range 1–6510) (11 skin cancers; 7 PTLD; 23 solid organ) ($p = 0.031$). Being older at transplantation, higher CNI exposure, Epstein-Barr virus negative status at transplantation, and no exposure to EVR were independent risk factors for NOPTM.

BO420 COMPLEMENT INHIBITION IN ANTIBODY MEDIATED REJECTION DURING KIDNEY TRANSPLANTATION

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Background: There is to date no gold standard treatment of antibody mediated rejection (AMR). Current therapeutic strategies rely on plasmapheresis combined with intraveinous globulins (IVIg). Eculizumab (ECmab) is a monoclonal antibody that targets C5 protein to prevent the membrane attack complex formation. Few clinical cases describe the efficiency of Eculizumab in treating acute AMR.
Methods: We conducted a monocentric retrospective study of 14 patients (7 men and 7 women) that have been treated between October 2011 and June 2013 for severe AMR using eculizumab on top of plasmapheresis, IV Ig and a B-cell targeting agent. Patients were transplanted between January 2002 and November 2012. All AMR were documented by a graft biopsy according to the Banff 2011 criteria at diagnosis and we report patients and graft outcome after treatment. The biopsy was repeated whenever necessary.
Results: The mean follow up was 16.4 months. Complement inhibition was fullfilled in both treatment groups throughout follow up. 8 patients out of 15 (53%) did not respond to the treatment and 6 lost their graft. 9 patients were diagnosed with AMR 27.2 months after their transplantation, out of which 7 (78%) did not respond to treatment. The remaining 6 were diagnosed with AMR in the first year following transplantation and only one lost his graft (17%), $p < 0.05$. Four patients had DSA but no C1q DSA. Three of them didn't respond to the treatment and only one had a favourable course. We found an equal propotion of patients with C1q DSA among responders (two out of 6) and non responders (three out of 8). In the responders group, the mean serum creatinine was 205 μmol/l 37.6 months after transplantation and 10.4 months after AMR diagnosis. No responding patients received eculizumab more than 3 months.
Conclusions: Eculizumab seems more efficient in early versus late AMR, which reflects a more prominent involvement of the complement cascade in early versus late AMR.

025 LIVER

LBO01* HCV DIRECT ACTING ANTIVIRALS IN LIVER TRANSPLANTATION: PRE OR POST?

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Direct acting antivirals (DAA) have opened a new era in HCV-infected liver transplant (LT) patients, possibly both limiting the need for a targeted Donor/Recipient match and improving long-term outcome. To investigate the impact of DAA on the early post-LT course we retrospectively analysed our prospective collected LT database since January 2014 to May 2015 focusing on HCV patients treated with DAA, regardless from the time of treatment. Twenty-six patients received Sofosbuvir associated with Peg-Interferon (2), Daclatasvir (1), and Ribavirin (23). Ten patients were treated before LT (Pre-DAA), 8 continued DAA across LT (Bridge-DAA), and 8 were treated after LT (Post-DAA). Patients were sorted according to HCV-RNA detection at the time of LT: 12 negative (HCVn) and 14 positive (HCVp). No differences in recipients and donors characteristics were present other than baseline HCV RNA levels which were lower in HCVn (346 076 vs. 4 436 657, $p < 0.05$). HCVn patients included all Pre-DAA and 2 Bridge-DAA, HCVp being composed by 6 Bridge-DAA and 8 Post-DAA. In average, negativization occurred 61 days pre-LT in HCVn and 59 days post-LT in HCVp ($p < 0.05$). Negativization time (days from DAA start to HCV-RNA negativization) was lower in HCVn (32 vs. 42, $p < 0.05$). LT course differed between HCVn and HCVp patients in the rates of both the grade (median Clavien-Dindo 2 vs. 3) and the severity of complications (Clavien-Dindo grade $\geq$ 3: 3 vs. 13). HCVp patients experienced a greater number of DAA-related side effects, especially leukopenia and anemia. HCV DAA in LT setting seems to significantly impact on LT morbidity. HCV-RNA negativity at LT seems to reduce transplant morbidity. We suggest that pre-LT and bridge DAA therapy should be preferred in LT patients. Our results need to be confirmed in large experiences.

LBO02* HEPATIC EPITHELOID ENDOTHELIOMA AND LIVER TRANSPLANTATION: THE ELITA-ELTR EXPERIENCE

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Background: The therapeutic algorithm of hepatic epithelioid endothelioma (HEHE), a rare low-grade vascular tumor, is still much debated mainly due to the lack of large detailed clinical experiences.
Methods: Analysis of 136 adult patients reported to the ELTR in order to define the value of liver transplant (LT) in the treatment of this disease. Neo-adjuvant treatment was performed in 39 (29%) patients. Thirty-eight (28%) patients had extra-hepatic disease (EHD) localization before LT. Fourteen (37%) of them had neo-adjuvant (4 = surgical, 6 = medical, 4 = both), 6 (16%) adjuvant (surgical = 1, medical = 3, both = 2) and 16 (42%) additional surgery during LT. Median FU from moment of LT was 63 mo (IQR = 22–125).
Results: Recurrent disease occurred in 36 (27%) patients after a median time of 18 mo (IQR = 8–73); 25/36 (69%) of them died after a median time from HEHE recurrence of 3 mo (IQR = 0–14). At Cox multivariable regression analysis, radiology-proven lymph-node invasion (rLNI) (HR = 4.521, $p = 0.008$), macro-vascular invasion (MVI) (HR = 3.074, $p = 0.013$) and waiting time (WT) before LT (HR = 0.840, $p = 0.018$) were predictors of recurrence. One-, 3-, 5- and 10-year disease-free survival (DFS) rates from moment of LT for the whole series are 90, 81, 78 and 69%. rLNI (5-year DFS: 50 vs. 79%; $p = 0.022$), MVI (5-year DFS: 40 vs. 84%; $p = 0.001$), and WT $\leq$120 days (5-year DFS: 72 vs. 91%; $p = 0.017$) significantly influenced DFS whereas radiological EHD didn't. One-, 3-, 5- and 10-year overall survival (OS) rates from moment of LT for the whole series are 87, 78, 77 and 70%. Similarly to DFS, rLNI (5-year OS: 43 vs. 79%; $p = 0.036$), MVI (5-year OS: 52 vs. 82%; $p = 0.013$), and WT $\leq$120 days (5-year OS: 71 vs. 88%; $p = 0.019$) significantly influenced OS; again radiological EHD didn't.
Conclusions: The long-term results of this, worldwide largest, HEHE transplant series are excellent. rLNI, MVI and faster LT significantly influence survival rates. Most importantly HED is not an absolute contraindication for LT.

LBO03* INFLUENCE OF DONOR WARM ISCHEMIA TIME ON DEVELOPMENT OF ACUTE KIDNEY INJURY AFTER DCD LIVER TRANSPLANTATION

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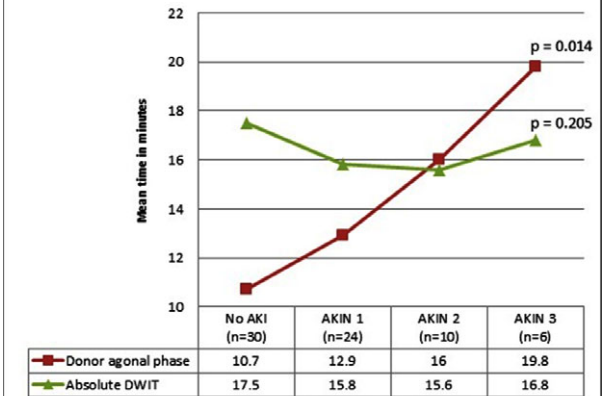
Introduction: Acute kidney injury (AKI) after liver transplantation (LT) is observed in over 50% of donation after circulatory death (DCD) recipients. This phenomenon has been attributed to the additional donor warm ischemia time (DWIT) with subsequent increase of hepatic ischemia/reperfusion injury (IRI). As of today various definitions of DWIT are used and little is known about its influence on the development of postoperative AKI. Our objective was to analyze the impact of DWIT on development and severity AKI after DCD LT.
Methods: Development of AKI, according to AKIN criteria, after DCD LT in our hospital was retrospectively assessed. DWIT was divided into two periods: donor agonal phase (time from saturation <80% or MAP <50 mmHg to asystole) and absolute DWIT (time from asystole to start of cold perfusion). Postoperative peak serum aspartate transaminase (AST) was used as a marker for hepatic IRI.
Results: Seventy DCD recipients were included of whom 40 (57%) developed AKI. Donor agonal phase was longer in the AKI group (15 vs. 11 min; $p = 0.020$). Surprisingly, absolute DWIT was shorter in the AKI group (15 vs. 18 min; $p = 0.050$). Donor agonal phase correlated well with severity of AKI (figure 1; $p = 0.014$) and this correlation was not observed for absolute DWIT ($p = 0.205$). After multivariable logistic regression of all clinical relevant donor, recipient, and intraoperative factors, agonal phase was independently associated with AKI (OR 1.104; 95% CI 1.014–1.203; $p = 0.023$). Also peak serum AST increased with length of donor agonal phase ($p = 0.002$), but was not congruent with absolute DWIT ($p = 0.374$).

Figure 1: donor warm ischemia and AKI severity



	No AKI (n=30)	AKIN 1 (n=24)	AKIN 2 (n=10)	AKIN 3 (n=6)
Donor agonal phase	10.7	12.9	16	19.8
Absolute DWIT	17.5	15.8	15.6	16.8

Severity of acute kidney injury

Conclusion: Our results suggest that not absolute DWIT, but donor agonal phase has an important influence on development and severity of AKI after DCD LT. Moreover the severity of hepatic IRI also increases with length of donor agonal phase. This study provides new insight on the importance of the donor agonal phase on the severity of AKI and hepatic IRI after DCD LT.

LBO04* A SCORE COMBINING ALPHA-FETOPROTEIN AND INFLAMMATORY MARKERS BETTER PREDICTS DROP-OUT AND RECURRENCE IN PATIENTS WITH HEPATOCELLULAR CANCER WAITING FOR LIVER TRANSPLANTATION

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Recently, growing interest has been observed on new variables able to refine the selection of patients with hepatocellular cancer (HCC) waiting for liver transplantation (LT). Alpha-fetoprotein (AFP) and inflammatory markers like platelet-to-lymphocite ratio (PLR) have been proposed in combination with morphological aspects as useful tools for identify new selection scores. The aim of the present study is to investigate a mathematical model combining biological and morphological aspects for the selection of HCC patients waiting for LT. Prospectively collected data of 208 HCC patients enlisted at St. Luc University Hospital Brussels during the period 1996–2012 were analyzed for the present study. Median intent-to-treat (ITT) follow-up for the entire population was 3.6 years (IQR: 1.0–7.8). Thirty-six (17.3%) patients dropped-out after a median time from waiting-list inscription of 6 months (IQR: 2–11). Fourteen on 172 (8.1%) transplanted patients recurred. At the moment of DO and LT, 13/36 (36.1%) and 8/172 (4.7%) patients exceeded radiological MC, respectively. At the moment of DO and LT, 6/36 (16.7%) and 2/172 (1.2%) patients exceeded AFP$\geq$1000 ng/ml. PLR$\geq$150 was more commonly observed in DO patients (27.8 vs. 19.2%). At multivariable analysis, pre-LT radiological MC-OUT status (OR 8.4, $p < 0.0001$), AFP$\geq$1000 ng/ml (OR 48.6, $p = 0.001$) e PLR$\geq$150 (OR 3.8, $p = 0.014$) were predictors of tumor-related DO and post-LT recurrence. Starting from these results, a mathematical equation was proposed: 2.127 (if MC-OUT) + 1.345 (if PLR$\geq$150) + 3.884 (if AFP$\geq$1000 ng/ml). Patients with a score $\geq$3 had a markedly inferior 5-year ITT survival (38.1%), and a significantly higher rate of post-LT recurrences (48.6 vs. 8.0%; $p < 0.0001$). Combination of biological and morphological aspects may

increase the ability of selecting HCC patients waiting for LT. Larger studies are needed with the intent to validate the proposed mathematical model.

LBO05* MELATONIN RESCUES SMALL FOR SIZE LIVER GRAFT FAILURE IN MICE

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Background: Living donor liver transplantation (LDLT) is impeded by small for size syndrome (SFSS). Melatonin is an endogenous hormone regulating biological circadian rhythm, it is also a hepatocyte protective agent and has strong antioxidant effect. The aim of the study is to investigate whether melatonin prevents SFSS by enhancing small liver graft regeneration and reducing graft ischemic injury.

Methods: Male C57BL6 mice were divided into 3 groups: (I) I/R+PH group: 60 min liver ischemia plus 2/3 hepatectomy; (II) I/R+exPH group: 60 min liver ischemia plus extended hepatectomy; (III) POLT group: 30% arterialized partial liver transplantation. Each group was subdivided into melatonin treated and control groups. Hepatic injury was determined by AST, ALT and histology. The cytokines and histological evidence of liver regeneration were examined by PCR and PCNA staining. Serum HMGB1 was measured by ELISA. Survival rate was monitored in I/R+exPH and POLT groups.

Results: Group I disclosed worse hepatic injury in control group compared with melatonin group. The livers of melatonin treated mice had increased regenerating hepatocytes by PCNA and PH3 staining as well as elevated levels of regenerative cytokines IL-6, TNF-α. HMGB1 was reduced significantly in mice treated by melatonin. In group II, 7 days' recipient survival rate was 0% in control mice in comparison of 50% in melatonin treated mice. In group III, the treatment of melatonin increased the survival rate of recipient mice from 0% in controls to 57% in melatonin group.

Conclusion: Melatonin rescues small for size liver graft failure by reducing ischemic reperfusion injury and promoting liver regeneration. The mechanism of the beneficial effect might be IL-6 dependent, but not biological circadian rhythm relevant.

003 CLINICAL IMMUNOSUPPRESSION & BIOLOGICALS

LBO06*

5 YEARS OF TACROLIMUS PRELOADING IN LIVE DONOR KIDNEY TRANSPLANTATION

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Background: Early rejection following live donor (LDKT) renal transplantation has been associated with lower tacrolimus levels in the first week. To address this problem, we routinely introduced tacrolimus preloading of the recipients from 4 days preoperatively. We audited the outcomes, 5 years following the introduction of this practice.

Methods: All patients undergoing live donor kidney transplantation were commenced on Tacrolimus 0.05 mg/kg BD from day 4 preoperatively. All patients were required to have their blood levels measured on the day of transplant, with a target level (TL) of 8–12 ng/ml. We performed a retrospective analysis of all LD transplants from Jan 2010 to Dec 2014. Primary end point: Tacrolimus levels week 1 post transplant; secondary end points: need for biopsy in 1st week, early rejection, incidence of delayed graft function (DGF) (12 ng/ml. Day 0 TL<8 was associated with more rejections (12.6% vs. 7%, $p = 0.6$) but did not affect 1 year eGFR (55 vs. 55.2 ml/min). DGF was associated with high TL (12.85 ± 6 vs. 9.5 ± 5.2, $p = 0.02$); DGF kidneys had lower eGFR at 3 months (38.1 ± 15 vs. 54.87 ± 18, $p = 0.0002$) but were improving by 12 months (44.8 ± 8.9 vs. 54.9 ± 19, $p = 0.09$).
Discussion: Tacrolimus preloading has its advantages, but with the routine use of antibody induction, its beneficial effect may be less pronounced. High preoperative TL is associated with lower eGFR, and this effect takes a few months to recover. Stringent audit of day 0 tacrolimus level is essential to avoid sub-therapeutic or toxic TL.

023 KIDNEY

LBO07*

EFFICACY AND SAFETY OF SOFOSBUVIR-BASED ANTI-VIRAL THERAPY TO TREAT HEPATITIS C VIRUS AFTER KIDNEY TRANSPLANTATION

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Background: There is no approved therapy for hepatitis C virus (HCV) infection after kidney transplantation, and no data regarding the use of new-generation direct anti-viral agents (DAAs) have been published so far. The aims of this pilot study were to assess the efficacy and safety of an interferon-free sofosbuvir-based regimen to treat chronic HCV infection in kidney-transplant patients.

Patients: Twenty-five kidney-transplant patients with chronic HCV infection were given for 12 ($n = 19$) or 24 weeks ($n = 6$): sofosbuvir plus ribavirin ($n = 3$); sofosbuvir plus daclatasvir ($n = 4$); sofosbuvir plus simeprevir, with ($n = 1$) or without ribavirin ($n = 6$); sofosbuvir plus ledipasvir, with ($n = 1$) or without ribavirin ($n = 9$); and sofosbuvir plus pegylated-interferon (PegasysÒ, Roche) plus ribavirin ($n = 1$).

Results: A rapid virological response, defined by undetectable viremia at week 4 after starting DAA therapy was observed in 22 of the 25 patients (88%). At the end of therapy, HCV RNA was undetectable in all patients. At 4 and 12 weeks after completing DAA therapy, follow-up data were available for 19 patients: all had a sustained virological response (SVR). The tolerance to anti-HCV therapy was excellent and no adverse event was observed.

Conclusion: New-generation oral DAAs are efficient and safe to treat HCV infection after kidney transplantation.

009 ETHICS/LAW/PSYCHOSOCIAL/PUBLIC POLICY

LBO08*

A LIAISON BETWEEN BUSINESS LEADERS, TRANSPLANT SPECIALISTS AND THE COMMUNITY TO LEAD CHANGES IN THE ORGAN DONATION SYSTEM IN AUSTRALIA -THE OUTCOMES MODEL

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Introduction: While proven leading practice in organ donation has been applied successfully by many nations, most developed countries still have deceased organ donor rates <25 donors per million population (DPMP). We hypothesised that application of business management tools might provide a solution to the supply problem.
Methods: The Outcomes Model (OM) was created to lead a problem-orientated solution for the benefit of the community albeit working outside usual systems. The OM used cross representative teams (all pro-bono) of business executives, experienced medical practitioners, politicians, and community leaders and utilized business principles to define the parameters needed to bring change and improved outcomes. OM begins with a comprehensive factual analysis that leads to a definition of World Leading Practice and then defines practical solutions including resources, project planning, effective management and targets.
Results: Australia's rate of 9.8 DPMP in 2006 had remained unchanged despite many initiatives over the previous 15 years. Following the Outcomes Australia initiative, the Australian Prime Minister, in 2008, approved a National Reform Package with more than AU$150 million over 4 years "to establish Australia as a world leader in organ donation". Although the organ donation rate in Australia in 2014 had improved to 16.1, it remains a long way from leading performance of 35 DPMP. Outcomes Australia, therefore, continues to advocate for complete implementation of leading practice in Australia.
Conclusions: Engaging business and community leaders and applying business principles has been instrumental in guiding a successful change process for organ donation systems
019 Ischemia/Reperfusion injury/Preservation
001 Allocation:

LBO09*

SURGICAL EXPERIENCE WITH NORMOTHERMIC MACHINE PERFUSION IN HUMAN LIVER TRANSPLANTATION

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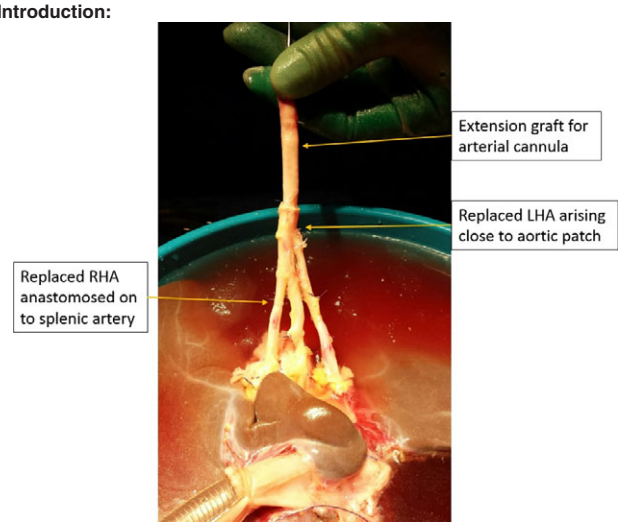
Introduction:



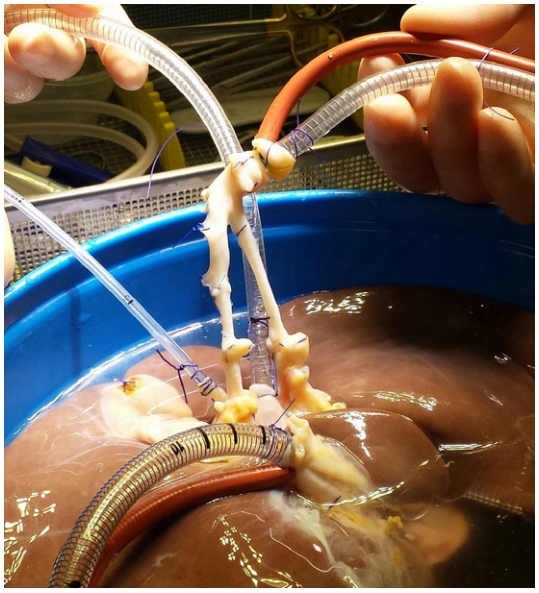
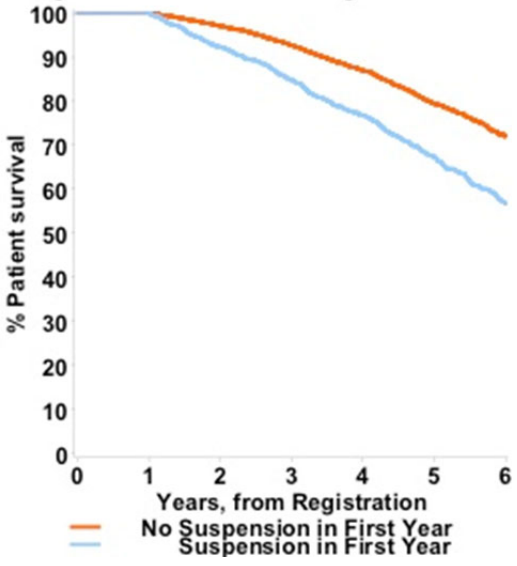


Figure 2- Patient Survival from Registration Date



Normothermic machine perfusion (NMP) offers a potential solution to the organ shortage crisis affecting liver transplantation. With the advent of any new procedure come new skills that need to be incorporated into clinical practice. We report the logistical impact and surgical techniques that have emerged related to the clinical use of NMP.
Methods: The OrganOx metra is a NMP device that perfuses a liver with oxygenated blood, nutrients and medications at 37oC to preserve it in a functioning state with the aim of improving organ quality. It requires the liver backtable to be performed at the donor hospital followed by cannulation of the hepatic artery (HA), portal vein (PV) and IVC before perfusing the organ. The NMP process continues during transport and storage until transplantation.
Results: Over 60 NMP-preserved livers have been successfully transplanted using this device. Organ cannulation has been identified as a critical step to achieve a successful perfusion.

The IVC cannula openings must be positioned directly over the hepatic veins to minimise episodes of IVC collapse which can compromise venous outflow. The PV must be dissected to the bifurcation to enable detection and prevention of twisting of the PV. Problems with each of these processes can prevent a successful perfusion.

Aberrant arterial anatomy was encountered in 30% of cases (19/64) requiring either arterial reconstruction to be performed at the time of retrieval (n = 10; image 1), or for the aortic tube to be excised intact with coeliac and SMA, enabling cannulation and perfusion directly through the aorta (n = 2; image 2). In 2 cases the distance between aortic patch and the origin of L HA was too short for cannulation, requiring the use of an extension graft (image 1).
Conclusion: NMP can be employed with all types of commonly encountered aberrant liver anatomy. A reasonable level of surgical expertise and meticulous cannulation technique are required for successful perfusion.

Suspension important event in life of patient waiting for kidney transplant affecting substantial proportion of patients on KTWL. Mortality of patients waiting for a kidney transplant higher than generally perceived when including SPt and the rate of suspension increases with time on KTWL. Survival benefit after DDRT similar between SPt and NSPt. Suspension in first year associated with inferior survival Age and cause of renal failure important risk factor for death and suspension.