BRIEF ORALS

Translational Kidney Immunology

BO001 EXPRESSION OF CXCR3 MONOCYTES INCREASES SIGNIFICANTLY IN THE GRAFT BLOOD COMPARED TO PERIPHERAL BLOOD IN PATIENTS WITH STABLE RENAL FUNCTION

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Introduction: We have recently reported that some lymphocyte populations do not maintain the same proportion in graft blood as in peripheral blood, despite a stable function of the transplanted kidney. These results suggest that the comparative study between leukocyte cells from the graft blood and those obtained in peripheral blood could provide information about the inflammatory state of the transplanted organ. In this work we selected the population of monocytes expressing CXCR3 to test this hypothesis.
Material and Methods: The study was performed by flow cytometry during the third, sixth and twelfth months after transplantation in 69 patients who received an isolated kidney transplant and the same immunosuppressive regimen. The peripheral blood sample was obtained by venipuncture and the graft blood by fine needle aspiration.
Results: We found a significant decrease in CXCR3 + monocytes throughout the first year of transplantation in peripheral blood (15.8 ± 20.7 vs. 12.6 ± 12.4 vs. 6.3 ± 9.0, p = 0.001), whereas the percentage of CXCR3 + monocytes in the graft blood did not change over this period. This situation resulted in a significant percentage difference between the CXCR3 + monocytes of the graft blood and those of the peripheral blood during the sixth (16.19 ± 9.54 vs. 12.6 ± 12.4, p = 0.027) and twelfth months (14.10 ± 8.94 vs. 6.3 ± 9.0, p < 0.001).
Conclusions: We can conclude, therefore, that the significant percentage increase of CXCR3 + monocytes in the graft blood with respect to the peripheral blood suggests the presence of inflammatory activity despite having stable renal function during the second half of the first year after transplant.

Basic Kidney Rejection

BO002 REJECTION TYPE ASSOCIATED COMPARTMENTAL DIFFERENCES OF MONOCYTE-MACROPHAGE KIDNEY ALLOGRAFT INFILTRATION

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Background: Rejection, regardless of the type and timing, significantly worsens the graft function and survival. Emerging evidence reveals a crucial role for the monocyte-macrophage lineage cells in the pathogenesis of rejection. Here, we studied monocyte-macrophage compartmental infiltration of 62 kidney transplant biopsies with the diagnosis of acute antibody mediated rejection (aABMR, *n* = 9), chronic antibody mediated rejection (cABMR, *n* = 13), acute cellular rejection type 1 (ACR I, *n* = 11) and acute cellular rejection type II (ACRII, *n* = 13), and 15 protocol biopsies from kidney transplants with stable function as the control group. Next we studied the relationship between these findings and allograft function and survival on the long term.
Material and Methods: We used immunohistochemical and immunofluorescent stainings to study monocyte-macrophage infiltration. Degree and intensity of infiltration was quantified by ImageJ analysis and laser scan confocal microscopy. Infiltrating monocytes were characterized by double staining with CD14 and CD16. Infiltrating macrophages were identified by expression of CD68, CD80, CD163 as follows: CD68 + CD80 (M1 type) and CD68 + CD163 (M2 type). Histopathological data was analyzed and correlated to eGFR, Creatinine and proteinuria levels on time of biopsy, 3, 6 and 12 months post-transplant.
Results: Overall, the presence of CD68 + macrophages in kidney biopsy is significantly associated with rejection compared to stable patients regardless of histopathological subtype (p=<0.01). Overall presence of CD68 + CD163 + macrophages is significantly associated with lower eGFR at the time of biopsy, 3, 6 and 12 months after rejection (p < 0.001). Glomerular infiltration by classical and intermediate monocytes and tubulointerstitial presence of non-classical monocytes were significantly associated with rejection regardless of rejection subtype (p=<0.01). cABMR is characterized by glomerular and tubulointerstitial CD68 + macrophages and gl.

Translational Liver Immunology

BO003 BILE DUCT REGENERATION AND IMMUNE RESPONSE BY PASSENGER LYMPHOCYTES SIGNALS BILIARY RECOVERY VERSUS COMPLICATIONS AFTER LIVER TRANSPLANTATION

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Background: This study aimed to elucidate the impact of epithelial regenerative responses and immune cell infiltration on biliary complications after liver transplantation.
Methods: Bile duct damage after cold storage was quantified by a BD damage score and correlated with patient outcome in 41 cases. Bacterial infiltration was determined by fluorescence in *situ* hybridization. Bile duct samples were analyzed by immunohistochemistry for E-cadherin, cytokeratin, CD56, CD14, CD4, CD8 and double-immunofluorescence for cytokine production and by mRNA microarray.
Results: Increased mRNA levels of adherens-junctions ($p < 0.01$) were detected in damaged bile ducts from patients without complications compared to damaged bile ducts from patients with biliary complications. Immunohistochemistry showed increased expression of E-cadherin and cytokeratin in bile ducts without biliary complications ($p = 0.004$; 0.002). Fluorescence in *situ* hybridization analysis demonstrated translocation of bacteria in bile ducts, however, mRNA analysis suggested an enhanced immune response in bile ducts without biliary complications ($p < 0.01$). Regarding immune cell infiltration, $CD4^+$ and $CD8^+$ cells were significantly increased in patients without complications compared to those with complications ($p = 0.016$; 0.008).
Conclusions: Following bile duct damage during cold storage, we hypothesize from our data that the functional regenerative capacity of biliary epithelium and enhanced local adaptive immune cell infiltration are crucial for bile duct recovery. Such molecular immunological bile duct analyses therefore could help to predict biliary complications in cases of "major" epithelial damage after cold storage.

Translational Cell Immunology

BO004 ANTI-HLA ANTIBODIES IN POOLED HUMAN SERUM DO NOT PREVENT DEVELOPMENT OF HUMAN REGULATORY MACROPHAGES FROM MONOCYTES IN CULTURE

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Background: A GMP-compliant process for manufacturing a medicinal cell-based product, known as Mreg_UKR, containing human regulatory macrophages (Mreg) has been established. Mreg_UKR is currently being investigated in a Phase-I/II trial as a means to safely reduce maintenance immunosuppression in kidney transplant recipients. Partway into this study, manufacturing failure occurred in 3 independent batches. These failures could not be attributed to procedural errors or donor-related factors. Therefore, a root-cause analysis was undertaken, including characterising current and previous lots of pooled, heat-inactivated, recalcified plasma-derived, male-only human AB serum that were used in the manufacturing process.
Methods: Single Ag bead arrays and CDC-crossmatches were performed by an accredited laboratory.

Results: Throughout process-development and clinical production, 3 separate charges of serum from the same supplier were used. Under research conditions, all 3 sera supported normal development of Mregs from monocytes. To test whether antibodies in the sera could explain idiosyncratic manufacturing failures, the 3 sera were screened by single-antigen bead array for anti-HLA. All 3 charges contained HLA Class I- and II-reactive antibodies at above-threshold levels. To test whether these antibodies fixed complement, mixed- and B cell-crossmatches were performed using cells from a DR4-positive donor. Despite the presence of anti-DR4 antibody, no complement-dependent cytotoxicity was observed. A low concentration of anti-HLA antibody in our AB serum is the most likely explanation for this discrepancy; however, we cannot formally exclude false-positive signals from the bead array or false-negative results from crossmatching.
Conclusion: The unexpected presence of anti-HLA antibodies in certain commercially available human AB sera argues for substituting human AB serum with platelet lysate or serum-free medium wherever feasible.

Translational Kidney Immunology

BO005 PATHOGENIC ROLE OF ANTI−HLA ANTIBODIES ON ENDOTHELIAL PROGENITOR CELL DYSFUNCTION IN HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Anti-HLA antibodies (ABS) bind to kidney graft endothelial cells inducing complement-mediated injury (CMI) and humoral rejection. endothelial progenitor cells (EPC) are bone marrow-derived precursors able to accelerate tissue regeneration through paracrine mediators such as growth factors and extracellular vesicles (EV), microparticles involved in cell-to-cell communication through horizontal rna transfer. aim of the study: to evaluate the potential anti-hla abs role on epc dysfunction in highly sensitized kidney transplanted (kt) patients.
Methods: Enrolled 20 kt patients with virtual PRA >80% characterizing anti-HLA abs. circulating EPC: evaluated by FACS (CD34 + /CD133 + /flk-1 + cells) and isolated on fibronectin-coated plates studying cmi, apoptosis and angiogenesis. in epc supernatants, vegf release was evaluated and ev were isolated and characterized for RNA content.
Results: In comparison to control kt patients without anti-HLA abs (n = 10), highly sensitized patients presented an increased circulating cd34 + / cd133 + /flk-1 + epc number. isolated epc showed decrease of proliferation and vegf production. also ev concentration, size and rna content was different from those isolated from control group epc with reduction of pro-angiogenic, anti-apoptotic and complement inhibitor mRNAs (BCL-XL, ENOS, AKT, CD55, CD59, factor h) and micrornas (MIR-126, MIR-296).

When incubated with plasma collected from highly sensitized kt but not control kt, epc showed enhanced CMI, apoptosis and a reduced angiogenesis activity. these detrimental effects were enhanced by co-incubation with vascular uremic toxins and by other microvasculature toxic molecules.
Conclusion: EPC of highly sensitized kt showed several functional alterations induced by anti-hla abs that may be responsible for decreased vascular repair during humoral rejection with consequent graft loss due to endothelial rarefaction. this detrimental effect may enhance endothelial injury due to common cause.

Basic Kidney Immunology

BO006 HLA-DQ ALLOANTIBODIES AND PERSISTENT INFLAMMATION SYNERGIZE TO DISRUPT ENDOTHELIAL CELL-MEDIATED EXPANSION OF REGULATORY T LYMPHOCYTES

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Antibody mediated rejection is characterised by microvascular inflammation, circulating Donor-Specific Antibodies (DSA) and endothelial lesions. We evaluated the outcome of HLA-DQ DSA binding to endothelial cells and the consequences on endothelial-lymphocyte interactions in a highly inflammatory environment.

A short exposure to IFNγ is sufficient to result in HLA-DQ^{neg} HLA-DR^{+} activated human microvascular endothelial cells (aEC), whereas sustained stimulation with IFNγ and TNFα was required for HLA-DQ^{+} HLA-DR^{++} highly activated endothelial cells (haEC). DSA were isolated from alloimmunized patients and characterised by Luminex assay. Intracellular signal transduction was determined by immunoblotting. To assess the functional value of endothelial activation, aEC and haEC were co-cultured with allogeneic PBMC, thereafter the polarisation of CD4^{+}-T cell subsets was identified by intracellular cytokine staining.

The presence of intragraft Th17 correlates with shorter graft survival, whilst the proportion of Treg cells has been implicated in tolerance. Previously, we found that aEC are capable of expanding Th17 and FoxP3^{hi} T regulatory cell (Treg) populations (Taflin PNAS 2011, Lion Am J Transplant 2016). We now report that allogenic haEC retain the ability to expand the pro-inflammatory Th1 and Th17 subsets, however their capacity for anti-inflammatory memory and naïve Treg expansion is abrogated. Notably early upregulation of FoxP3 in CD4 + T cells is stunted in haEC cocultures. HLA-DQ DSA binding to haEC initiates rapid and transient phosphorylation of AKT and S6K. Moreover, HLA-DQ DSA further reduced differentiation of the memory FoxP3^{hi} Treg subset in haEC cocultures.

Endothelial cells exposed to inflammation have a selectively reduced capacity to expand the CD4 + Treg subpopulations; an effect that is compounded by the presence of HLA-DQ DSA. This reduction in anti-inflammatory cells likely exacerbates allograft damage and reduces tolerance efficiency.

Translational Cell Immunology

BO007 EFFECT OF ALLOGENEIC MESENCHYMAL STEM CELLS ON IMMUNE REJECTION AGAINST XENOGENEIC CHONDROCYTES INJECTED IN THE RAT JOINT

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Background: Most patients with cartilage defects produced by traumatism or disease do not benefit from a good therapeutic solution. Notably, cellular therapies may provide a cure for such lesions if the appropriate cell type is utilized. Here, we consider the use of xenogeneic chondrocytes for cartilage repair and allogeneic mesenchymal stem cells (MSC) for immune modulation.
Methods: A discordant xenotransplantation model was established by injecting three million porcine articular chondrocytes (PAC) into the femorotibial joint of Lewis rats to monitor the immune response over time. The biodistribution and immunoregulatory effect of systemic administration of bone marrow-derived MSC obtained from Wistar rats was assessed in this model. MSC were administered either intra-venously (i.v.) one week before PAC injection or intraperitoneally (i.p.) 3 weeks after.
Results: Anti-PAC IgM and IgG responses were detected in all PAC-injected rats with a peak at week 2 post-injection and reactivity remaining above baseline levels by week 18. IgG2a and IgG2b were the predominant and long-lasting IgG subtypes. Consistent with a cellular immune response to PAC, a distinct cytokine/chemokine profiling was revealed in serum by antibody array relative to controls. This was characterized by elevation of multiple markers at week 2, as well as increases in cell numbers in draining lymph nodes.

Interestingly, IL-2 measurements in co-cultures of rat peripheral blood lymphocytes (PBL) with PAC indicated that PAC injection induced some T-cell hyporesponsiveness. However, allogeneic MSC administered systemically either 1 week before (intravenous route) or 3 weeks after PAC injection (intraperitoneal route) did not diminish the immune response against PAC. Thus, tolerance was not enhanced in these cohorts.
Conclusions: PAC injected intra-articularly in rats induced a cellular and humoral immune response. This effect was not counteracted by systemic administration of MSC.

Basic Heart Immunology

BO008 CD16/FCγR PROFILING ALLOWS NON INVASIVE APPRAISAL OF ANTIBODY-DEPENDENT NK CELL ALLOREACTIVE POTENTIAL IN HEART AND KIDNEY TRANSPLANT RECIPIENTS

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Background: Identification of risk factors that stratify the level of humoral risk is essential to adapt individualized therapy and favor graft survival after solid organ transplantation. Gene profiling in AMR biopsies identify the potential value of Natural Killer (NK) CD16 and CX3CR1 transcripts to refine diagnosis of allograft rejection, but little is known about their role in promoting allograft vasculopathy. This study aimed to investigate whether CX3CR1 and CD16 peripheral NK cell profiles may be associated to allograft dysfunction in kidney (KTR) and heart (HTR) transplant recipients.
Methods/Materials: Flow cytometry analysis of peripheral blood CD16 and CX3CR1 NK cell phenotype and cytotoxic function was conducted in 148 KTR and 103 HTR. A functional NK-cellular humoral activation test (NK-CHAT) was used to evaluate the CD16 and antibody-dependent cytotoxic activity of recipient NK cells in response to rituximab. Link between CX3CR1 and CD16 markers profiles and allograft dysfunction were tested in multivariate analysis.
Results: High inter-individual variability of CX3CR1 and CD16 phenotypes and FcgR-dependent cytotoxic activation of NK cells was observed in transplant recipients. Enhanced NK cell responsiveness was identified as an independent factor predicting development of cardiac allograft vasculopathy or decline in kidney allograft function. We further show that NK-CHAT evaluation of CD16/FcgR receptor engagement can index the complement independent cytotoxic potential of circulating DSA towards allogeneic targets in vitro.
Conclusion: Collectively, our study suggests that the integrated analysis of CD16 and DSA profile in transplant recipients may stratify patients at higher risk to elicit NK-cell-mediated allograft vascular damage in response to chronic alloantibody challenge. This study points out to the clinical potential of such non invasive NK–CHAT immunomonitoring to orient NK-cell targeted therapies in high NK-responsive recipients.

Basic Kidney Rejection

BO009 DUAL TREATMENT OF SUBOPTIMAL DOSES OF CSA AND MSC INFUSION FULLY PREVENTS ACUTE REJECTION IN AN ALLOGENIC MODEL OF RENAL TRANSPLANTATION

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The immunomodulatory characteristics of mesenchymal stem cells (MSC) may lead to multifaceted strategies in transplantation organ rejection. This study was designed to investigate the immunosuppressive effects of the donor-type MSCs infusion from Wistar rats to Lewis rats in a renal transplantation model of Wistar to Lewis.

Rats were allocated into different groups: Non-Treated ($n = 10$); Cyclosporine group (CsA) treated daily with 5 mg/kg ($n = 9$); CsA" group treated daily with 2.5 mg/kg, a suboptimal therapeutic dosage ($n = 5$); MSC group treated with two intravenous injections, at day −7 and 0 ($n = 8$) and MSC + CsA" group which combines suboptimal CsA and MSC infusion ($n = 8$). Heterotopic renal transplantation was performed from Wistar to Lewis with a 21 days follow-up.

Serum creatinine was measured: MSC treated group displayed a significant reduction of creatinine in contrast to Non-Treated group. Combining the subtherapeutic dose of CsA with MSC, the reduction was greater improving values of the CsA1/2 group. We also saw differences in the mean survival time (MST), which was 12.4 days ±4.2 in the Non-Treated group. Both CsA and CsA" + MSC were 21 days in all animals. MSC group significantly increased the MST up to 18.5 days ±4.1. CsA and CsA" + MSC group showed 100% of survival, in Non-treated was 13.3% and suboptimal dose of CsA and MSC treated group was 60% and 50% respectively.

Histopathology analysis at the end-point in Non-treated rats showed severe inflammatory cell infiltration accompanied by glomerular and acute tubular necrosis. Although CsA1/2 + MSC group, displayed a reduction in the inflammatory markers, glomerular and acute tubular necrosis were strongly reduced being the global score significantly reduced in contrast to Non-treated group.

In conclusion, MSC infusion shows an immunomodulatory effect but dual therapy with MSC infusion and suboptimal doses of conventional immunosuppressors offers a full immunological protection in the model of renal allotransplantation.

Basic Liver Immunology

BO011 DIFFERENT KINETICS OF HEPATOCYTE AND CHOLANGIOCYTE REGENERATION BY RECIPIENT EPITHELIAL (STEM) CELLS AFTER LIVER TRANSPLANTATION

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Introduction: Liver graft regeneration is relevant for transplantation outcome. Impaired regeneration has been linked to post-operative complications including non-anastomotic bile duct strictures (NAS). It has been hypothesized that recipient-derived (stem) cells may contribute to regeneration of damaged grafts and thereby establishing epithelial chimerism. The aim of this study is to determine the extent and kinetics of recipient-derived hepatocytes and cholangiocyte repopulation after retransplantation (reLTX).
Methods: All reLTx between 2001 and 2015 were included and selected for HLA-A2 or sex miss-matches between donor and recipient. Recipient-derived cells in explant liver graft were identified using immunohistochemistry for HLA-A2, X- and Y-chromosome fluorescent in situ hybridization (FISH) and stem cell derived liver organoid cultures.
Results: 13 HLA-A2 negative explants in HLA-A2 positive recipients were included in this study, of which five for NAS. Median time until re-transplantation was 167 (2–2879) days all grafts, extensive repopulation of hepatocytes and cholangiocytes by recipient cells was observed. These results were confirmed by XY-FISH analysis in four female grafts transplanted in male recipients. A significant difference in HLA-A2 positive hepatocytes was observed between early and late reLTx (<1 month mean 8.3% ± SD 6.4 vs. 31.8 ± 23.5% > 12; $p = 0.03$). In contrast, the percentage of recipient derived cholangiocytes was not time-dependent (10.8 ± 12.9% vs. 8.5 ± 8.5%; $p = 0.75$). No clear differences in hepatocyte repopulation was observed between NAS and the non-NAS group (11.8 ± 9.6% vs. 26.0 ± 27.2%; $p = 0.38$) though there was a clear trend toward more cholangiocyte repopulation by host cells in the NAS livers (13.8 ± 12.7% vs. 3.5 ± 4.4% $p = 0.054$).
Conclusion: Extensive epithelial chimerism occurs after liver transplantation. The kinetics of hepatocyte and cholangiocyte chimerism is significantly different, suggesting distinct underlying regenerative mechanisms.

Basic Heart Rejection

BO012 MOLECULAR CORRELATES OF ENDOTHELIAL MTOR ACTIVATION IN HEART TRANSPLANT RECIPIENTS

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Background: The detection of phosphorylated effectors of the mTOR pathway such as phosphorylated-S6RP in endothelial cells by immunohistochemistry (IHC) has been associated with Antibody-Mediated allograft Rejection (AMR). The aim of this study was to evaluate the molecular phenotype related to the endothelial detection of pS6RP in heart transplant recipients.
Methods: This case-control study included 41 heart transplant patients from four French referral centers with biopsy proven antibody-mediated rejection (pAMR+) and a matched control group of 30 patients without rejection (pAMR0) based on the updated ISHLT classification. From these patients, 94 endomyocardial biopsies (EMB) had adequate material for microarray analysis and endothelial expression analysis of pS6RP by IHC. We also determined the allograft gene expression profile using the ABMR molecular score in addition to pathogenesis-based transcripts reflecting endothelial activation (DSAST and ENDAT), macrophage burden (QCMAT), gamma-interferon response (GRIT) and NK-cell burden (NKB) (http://atagc.med.ualberta.ca).
Results: Among the 94 EMBs included in the main analyses, 50 were pAMR+ (53.2%) and 44 (46.8%) were pAMR0 normal EMBs. Endothelial expression of pS6RP was observed in 27/50 (54%) of pAMR+ biopsies and 12 out of 44 normal biopsies (27.3%, Fischer's exact: $p = 0.012$). As compared with biopsies without pS6RP labeling, biopsies with pS6RP staining showed increased expression of DSAST (Mann-Whitney: $p < 0.0001$), ENDAT ($p = 0.0009$), QCMAT ($p = 0.0046$), NKB ($p = 0.0001$), GRIT ($p = 0.0008$) and increased ABMR molecular score reflecting AMR injury ($p = 0.0001$).
Conclusion: Endothelial activation of mTOR pathway is associated with AMR and increased expression in transcripts reflecting endothelial activation, macrophage burden, microcirculation and NK burden. Our results suggest the importance of the mTOR pathway activation in AMR injury and the potential interest of using mTOR inhibitors in this setting.

Basic Others Immunology

BO013 MYD88 SIGNALING IN TREGS IS REQUIRED FOR DIFFERENTIATION INDUCED BY ALLOGENETIC SERTOLI CELLS

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Background: Testicular Sertoli cells (SCs) play a major role in the immune-privileged environment. It is proved that primary SCs isolated from testis protect cotransplanted allogeneic and xenogeneic cells from rejection in animal models. The mechanisms responsible for immune privilege are complex, considered to be related to SCs inducing Treg differentiation. Naïve T cells or pre-T cells influenced by SCs undergo further differentiation into an activated state that highly expresses genes critical for Treg function, although how this process proceeds on a molecular level is poorly understood. It is reported that Treg-cell-specific deletion of the Toll-like receptor (TLR) adaptor myeloid differentiation factor 88 (MyD88) resulted in deficiency of Tregs. Here, we detect that MyD88 is required for differentiation of Tregs induced by SCs. Methods and Materials Primary SCs were isolated from BALB/c mice testis and cultured in 6-well plate, >97% purity. CD4 + CD8 + double positive precursor T cells were sorted from C57BL/6 mice thymocytes and co-cultured with allogeneic SCs. Number and effect of Foxp3 + Tregs were investigated to reveal SCs inducting CD4 + Foxp3 + Tregs differentiation. Furthermore, MyD88-deficient mice (MyD88−/− mice) were used to obtain MyD88−/− pre-T cells to investigate the role of the MyD88 pathway in this response. Results MyD88 is upregulated in Foxp3-expressing Tregs, co-cultured with allogeneic SCs. MyD88-deficient pre-T cells show lack multiple effector molecules (Foxp3, CD62L, TIGIT, KLRG1) and fail to differentiate into CD4 + Foxp3 + Tregs in the presence of SCs. MyD88-CD4 + Foxp3 + Tregs sorted from MyD88−/− mice spleen produce less IL-10, IL-35 and TGF-beta cytokines with allogeneic SCs co-culture. Conclusion Our findings demonstrate that MyD88 signaling renders pre-T cells differentiating into Foxp3 + Tregs induced by allogeneic SCs and contributes to Tregs regulatory function.

Basic Kidney Rejection

BO014 HYPOTHERMIC OXYGENATED PERFUSION (HOPE) – A SIMPLE AND EFFECTIVE METHOD TO MODULATE THE IMMUNE RESPONSE FOLLOWING KIDNEY TRANSPLANTATION

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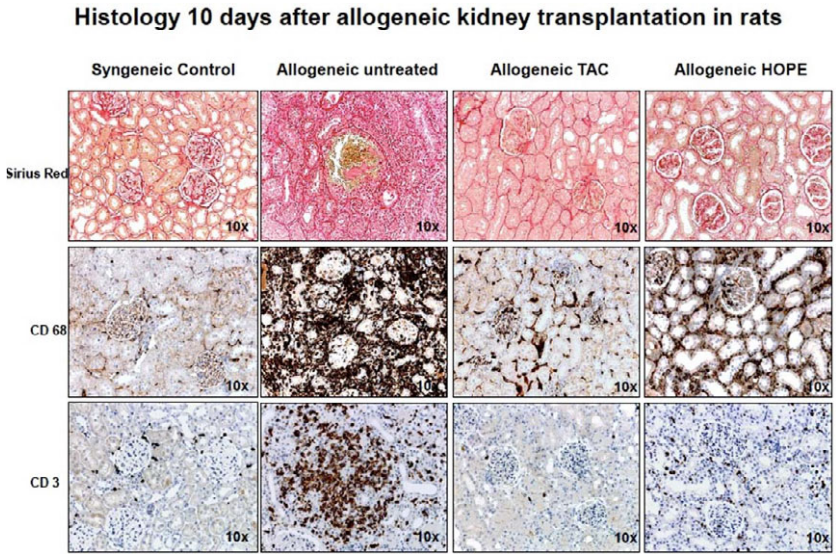
Objective: To investigate the impact of HOPE on the immune response following kidney transplantation in an allogeneic rodent model.
Background: Hypothermic Oxygenated PErfusion (HOPE) has a strong beneficial impact on organs through repair of mitochondrial pathways. Downstream effects include also modification of the innate immune response after transplantation. We therefore aimed to test HOPE in a model of allogeneic kidney transplantation.
Methods: Kidneys from Lewis rats were transplanted into Brown Norway rats to trigger severe rejection in untreated recipients. In a second group, Brown-Norway recipients were treated with tacrolimus, whereas in a third group the kidney grafts were solely pretreated with 1 h HOPE before implantation, and recipients received no immunosuppression at all.
Results: Allogeneic kidney transplantation led to death in untreated recipients within 14 days after transplantation, due to acute rejection. Tacrolimus treatment prevented acute rejection, and improved significantly survival. In the third group, HOPE treatment, without any additional immunosuppression, decreased graft injury and protected grafts from severe lethal immune response, as assessed by T-Cell activation (CD3) and macrophage activation (CD68). ELISA analysis of plasma Il6, Il10, 8OHdG, HMGB-1, TLR-4 and Fluorescence activated Cell sorting (FACS) confirmed these results.
Conclusion: This is the first study demonstrating the beneficial effects of HOPE on the immune response following kidney transplantation in an allogeneic rodent model. HOPE treatment significantly decreased the immune response and prevented rejection following transplantation.



Clinical Kidney Donation and donor types

BO015 ALTRUISTIC NON-DIRECTED LIVING KIDNEY DONATION: TRANSFORMING LIVING DONOR KIDNEY TRANSPLANTATION IN THE UK

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Introduction: A new legal framework enabled altruistic non-directed donation to start in the UK in 2006. Kidneys were initially only allocated to suitable recipients on the deceased donor waiting list, but in 2012 altruistic donors (AD) had the option of donating into the kidney paired donation (KPD) pool to create an altruistic donor chain of two or (since 2015) three transplants in the UK living kidney sharing schemes (UKLKSS).
Methods: The demographic and activity data of AD are summarised.
Results: Potential AD are evaluated using national clinical guidelines, including mandatory mental health assessment. Once fully assessed, AD are registered with NHS Blood and Transplant and a suitable recipient is identified on the waiting list or they join the next quarterly matching run of the UKLKSS, which also identifies KPD transplants. Anonymity is required before transplantation and is only broken thereafter if both parties agree.

By the end of 2016, 548 AD had donated a kidney. Mean donor age was 54 years (range 20–85 years); 52% were male. The median interval between identifying a recipient and donation was 51 days with >80% donating within 90 days. Kidneys not donors were transported, with median cold ischaemia time of 6 h.

Of the 456 AD from 2012 on, 361 (79%) donated to the waiting list, with 95 (21%) donating into the KPD pool and generating 213 transplants through chains (118 for pool recipients and 95 for waiting list recipients).
Conclusions: A successful national programme for altruistic living kidney donation in the UK has enabled 666 recipients to benefit from a living donor transplant generated by 548 AD. When AD donate into the UKLKSS, three transplants can be created from a single donation and consequently, AD generated 12% of all living donor kidney transplants in the UK last year. In particular, this has had an impact on the most immunologically complex recipients, resulting in a reduction in antibody incompatible transplantation in the UK.

BO016 SHORT TERM POSTOPERATIVE OUTCOMES IN LIVING DONOR KIDNEY TRANSPLANT DONORS

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Background: Living Donor Kidney Transplantation is the treatment of choice for End-Stage Renal Disease. Nephrectomy bears certain shortterm risks. Some eligible donors suffer from obesity which can impair short-term postoperative outcomes. Therefore, we assessed short-term perioperative outcomes according to BMI in our institution.
Methods: We identified $n = 289$ patients that underwent unilateral donor nephrectomy between JAN/2006-DEC/2015. Groups were analyzed according to their BMI (BMI <25 kg/m², BMI ≥25 / <30 kg/m², BMI ≥30 kg/m²). The retrospective study was approved by the institutional review board (EK 1887/2016).
Results: $N = 126$ donors had a BMI <25 while $n = 120$ had a BMI ≥25/<30 and $n = 43$ a BMI ≥30. BMI had no statistically significant influence on the percentage of laparoscopic donations (86.5% vs. 81.7% vs. 86%, p=n.s.) or on conversion rates (0% vs. 2.0% vs. 2.7%, p=n.s.) as well as on postoperative complication rate (8.7% vs. 13.3% vs. 14.0% Clavien-Dindo Grade II complications in BMI <25, BMI ≥25 and <30 and BMI ≥30, respectively). There was no difference in pre-OP kidney function, post-OP Surgical Site Infection or Systemic Infection. Kidney Function after Surgery decreased statistically significant after the donation and did not recover until the time of discharge (eGFR -23.55 ml/min (±0.88) vs. -23.91 (±0.90) and -25.77 (±1.44)). Donors with BMI≥30 showed a significantly higher reduction in eGFR compared to BMI <25 and BMI ≥25 / <30 (Relative decrease of 27.7 (±0.9)%, 29.3 (±0.9)% and 45.8 (±2.4)%, p=<0.0001).
Conclusion: Obese patients do not suffer from a higher risk of postoperative complication rates but show a more pronounced relative decrease in kidney function postoperatively until discharge, eventually due to a lower "reserve" because of a worse nephron/BMI ratio. Obese donors might require closer postoperative short-term monitoring. Data need to be validated in larger donor cohorts.

BO017 RATE OF KIDNEY FUNCTION DECLINES MORE IN KIDNEY DONORS AGED OVER 65 YEARS

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Background: Living kidney donation from older individuals has become more common due to the shortage of cadaveric donors in Japan. Given the strong association of older age and chronic kidney disease with cardiovascular disease (CVD), kidney donation from old individuals may cause an increase of CVD and death.
Methods: To evaluate the safety of living kidney donation from older individuals, we performed a retrospective single center cohort study among kidney donors who underwent donation between 2009 and 2016 at our institution. We divided them into two groups (OLD: older living donor aged ≥65; YLD: younger living donor aged <65) and analyzed the rates of mortality and CVD events, decline of estimated glomerular filtration rate (eGFR), proteinuria, and the rate of new-onset comorbidities such as hypertension (HT), dyslipidemia (DL), hyperuricemia (HUA), and diabetes mellitus (DM) at 12 months.
Results: Among 141 living donors, 82 (OLD:20, YLD: 62) had available data at 12 months after donation. The baseline eGFR was 77.0 ± 15.9 ml/min/1.73 m^2 in OLD and 81.1 ± 12.7 ml/min/1.73 m^2 in YLD ($p = 0.30$). No donor had died or developed CVD within 12 months. When compared with donors in YLD, donors in OLD had a significantly higher rate of eGFR decline (ΔeGFR/baseline-eGFR) (42.0 ± 5.7% in OLD, 37.6 ± 7.4% in YLD; $p = 0.005$). No donor developed proteinuria (urine dipstick ≥±) within 12 months. There were no significant differences between the groups in the rate of new-onset HT (6.7% in OLD versus 5.8% in YLD ($p = 1.00$)), DL (18.2% in OLD versus 20.8% in YLD ($p = 0.67$)), HUA (10.0% in OLD versus 12.7% in YLD ($p = 0.62$)) and DM (5.2% in OLD versus 0% in YLD ($p = 0.24$)).

Conclusion: This study demonstrated that nephrectomy for donors aged over 65 was associated with a higher eGFR decline rate at 12 months post-donation. Long-term follow-up is necessary to maintain residual kidney function and monitor CVD risks such as HT, DL, HUA, and DM.

BO018 RADIOISOTOPIC EVALUATION OF RENAL FUNCTION IN KIDNEY TRANSPLANT DONORS AFTER NEPHRECTOMY FOR DETECTION OF EARLY AKI AND LONG TERM COMPENSATORY RENAL HYPERTROPHY

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Background: After nephrectomy, as a result of the decrease of the nephron mass, kidney transplant donors (KTD) develop a partial loss of renal function (RF), defined as AKI (Acute Kidney Injury). The recovery of RF is mainly ascribed to renal reserve function (RFR), defined as the capacity of the kidney to increase GFR. There are only few studies on RFR in KDT and a correlation with long term functional outcomes.
Methods: 20 KTD renal function was analyzed before nephrectomy, in the immediate postoperative period and 1 year after.
Result: Mean KTD serum creatinine (sCr) was 0.73 mg/dl (0.5–0.96), eGFR (CKD-EPI) 97.7 ml/min/1.73 m^2 (69–119) and radioisotope (51Cr-EDTA) GFR 100 ml/min (78–129). The split function was evaluated by a concomitant scintigraphy using 99mTc-MAG: the mean percentage of RF of right kidney was 48.12% (43–56) and left 51.88% (44–57). As expected, immediately after nephrectomy all KTD worsened RF: the mean percentage increase of sCr was 81% (50–105%) within 72 h post-surgery (we observed the peak of creatinine after 24–48 h in the most of cases). 7 days after, renal recovery was observed in all cases: the mean percentage increase of sCr was 53.2%, significantly lower than the zenit of sCr. These results suggest a potential gain of about 30% in comparison to the starting value of the right kidney. One year after nephrectomy (all left nephrectomies), we studied KTD renal function (GFR) using a radioisotopic evaluation of RF using 51Cr-EDTA and we then compared it with the split radioisotope GFR of right kidney at the first scintigraphic evaluation. Mean GFR was 68 ml/min (50–87) vs 48.5 ml/min (40–60) before donation with an average GFR increase of 19 ml/min (0.5–46) and a percentage increase of the right RF up to 110% (mean 41%).
Conclusion: Radioisotopic evaluation is feasible and allows a precise determination of RF at different time points after nephrectomy. Compensatory hypertrophy was observed in all the 20 KTD independently from the presence of comorbidities.

BO019 SHOULD KIDNEY TRANSPLANTATION BE DONE FROM ELDERLY DONORS?

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Background: We aimed to evaluate graft survival and graft functions of patients who were renal transplanted from elderly donors (≥60 years).
Material and Methods: We included 2138 renal transplant patients who were transplanted from living donors between 2000 and 2016 years and divided to two groups. Group 1 (≥60 year donors): 234 patients (10.9%, M/F: 157/77, mean ages ± sd: (Recipients/Donors): 40.2 ± 12.8/ 65.2 ± 4.3), Group 2 (<60 year donors): 1904 patients (89.1%, M/F: 1331/573, mean ages ± sd: 37.3 ± 12.5/ 41.5 ± 10.1). There were no significant differences between the groups in terms of recipient genders, etiology of chronic kidney disease, lymphocyte cross match positivity and immunosuppressive protocols. The rate of basiliximab use for induction therapy was higher in two groups. Glomerular filtration rate (by DTPA) and length of kidney by ultrasonography were significantly lower in the Group 1 (42.9 ± 8.3/ 48.5 ± 10.7 ml/min, p: <0.001/ 107.2 ± 13/ 108.5 ± 14.8 mm, p: 0.002, respectively). SPSS 20.0 software program was used for statistical analysis.
Results: Graft (1/15 year, Group 1: 96–82%/ Group 2: 96–91, p: 0.515) and patients survival rates (0.313), delayed graft functions (p: 0.113), acute rejection (20.5%/26.9%, p: 0.796), cytomegalovirus (p: 0.475) and BK virus viremia (p: 0.721), new onset diabetes after transplantation rates and amount of proteinuria were similar between groups. Serum creatinine levels in last control were significantly higher in the group 1 (1.79 ± 1.5/ 1.28 ± 0.6, p: <0.001, respectively). Chronic allograft dysfunction rate was significantly higher in group 1 (9.4%/ 5.7%, p: 0.004).
Conclusion: Our study showed that elderly donors should be used for renal transplantation because of the early and long term graft and patients survival rates were similar to those from younger donors though serum creatinine levels were worse in group 1 and no significantly differences other important parameters.
Key words: Elderly donors, renal transplantation, graft survival

BO020 MARGINAL FACTORS AFFECT THE POSTOPERATIVE KIDNEY FUNCTION OF COMPLEX LIVING DONORS FOR KIDNEY TRANSPLANTATION

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Background: Recently, complex living donors with marginal factors including hypertension, dyslipidemia, glucose intolerance, and obesity are increasing. Postoperative kidney functions of living donors for kidney transplantation are of our great concern. We investigated the pathological findings of control biopsy and postoperative kidney functions evaluated with estimated glomerular filtration rates (eGFR) of the complex living donors with marginal factors.
Methods: Between January 2008 and June 2016, 752 living donors for kidney transplantation performed at Nagoya Daini Red Cross Hospital. Six hundred ninety eight of 752 were followed up more than 6 months after operation and included in this study. Marginal criteria for complex living donors include hypertension (>140/90 or treated with medications), dyslipidemia (LDL cholesterol >140 or treated with medications), glucose intolerance (impaired fasting glycemia, impaired glucose tolerance, or diabetes mellitus treated with medication within the range of HbA1c < 6.5% and albuminuria <30 mg/g·Cr), and obesity (BMI > 30 kg/m^2). Living donors were stratified into 3 groups with age (20–39 years, 40–59 years, and 60–79 years). Living donors with more than one marginal factor were classified into the group with marginal factors. Twelve of 41 living donors between 20 and 39 years, 179 of 312 living donors between 40–59 years, and 263 of 346 living donors between 60 and 79 years had more than one factor and were classified into complex living donors. Pathological findings of control biopsy and postoperative eGFRs in each stratified years were compared between complex living donors with marginal factors and healthy living donors without them, retrospectively.
Results: In pathological findings of control biopsies, obsolescent glomerulus or arteriolosclerosis were identified more significantly in the complex living donor.

BO021 DOES THE LOW BIRTH WEIGHT HAVE AN IMPACT ON LIVING KIDNEY DONORS OUTCOMES?

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Since nearly 30 000 people worldwide become a live kidney donor each year, donor safety is of the utmost importance. Recent papers indicate that living kidney donation is associated with an increased relative risk for end-stage renal disease (ESRD). It is essential to determine which donor will be more likely to develop ESRD. One of the risk factors for ESRD in live kidney donors is hypertension and as there are studies demonstrating that a low-birth weight (LBW) is a risk factor for developing hypertension in adult life, we hypothesized that donors with LBW may be at higher risk of developing renal disease after donation.

We examined our cohort of living kidney donors (n = 73) that underwent a laparoscopic left-sided donor nephrectomy that were followed up for at least 12 months, and 33 of them were observed for at least 24 months after donor nephrectomy. Donors were divided into 2 cohorts: a group with LBW, and a control group with normal birth weight (NBW). We decided to check whether the donor birth weight has an impact on the outcome of donor renal function and on the development of hypertension.

There was no difference of presence of pre-donation hypertension between LBW and NBW groups (p = 0.08). However, donors with LBW are more likely to present new-onset hypertension after donor nephrectomy (p = 0.049). GFR before kidney donation is significantly lower in the LBW group (p = 0.045), both for split renal function and total kidney function.

BO022 LEFT-SIDED DONOR NEPHRECTOMY PREDISPOSES LIVING KIDNEY DONORS TO LATENT ADRENAL INSUFFICIENCY WITH SYMPTOMS OF FATIGUE AND INFERIOR QUALITY OF LIFE

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The rising prevalence of ESRD and chronic organ shortage calls more people upon to consider living kidney donation. The risks of impaired quality of life, particularly symptoms of fatigue, however, remain less well understood and dampen enthusiasm.

We hypothesized that left-sided donor nephrectomy predisposes donors to symptoms of fatigue due to impaired blood supply of the left adrenal gland. We analyzed 356 living kidney donors from 1998 to 2013, and aimed to address the impact of donation on physical health and quality of life using the SSF-8 questionnaire. In addition, we prospectively followed 27 living kidney donors for symptoms of fatigue. Morning cortisol and ACTH levels were performed at baseline and +6 months post donation.

Using a standardized quality of life score, left-sided donors showed a significant worse quality of life ($p = 0.037$). Left-sided donors were more likely to develop symptoms of fatigue and less likely to develop hypertension ($p < 0.05$). Donors with fatigue were more likely to be younger and have physically and mentally demanding jobs ($p < 0.05$). Among our prospectively followed donors we identified 4/11 left-sided donors with self-reported fatigue compared with 1/16 right-sided donors. No differences were observed for morning cortisol and ACTH levels at baseline ($p > 0.05$). However, right-sided donors were more likely to show stable morning cortisol levels from pre to +6 months post donation, while left-sided donors showed a decline of morning cortisol levels ($p < 0.05$). While 5/16 right-sided donors developed hypertension post donation, no left-sided donor developed hypertension ($p = 0.059$).

Our results strongly indicate that the side of donor nephrectomy impacts long-term quality of life. Impaired function of the left adrenal gland due to transection of adrenal vessels may result in latent adrenal insufficiency with fatigue and less hypertension. The impact of side-selection may influence donor education and the surgical approach to donor nephrectomy.

BO023 GLOBAL KIDNEY EXCHANGE: A CASE STUDY

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Abstract: Organ shortage is the major limitation to kidney transplantation in the developed world. Conversely, millions of end-stage renal disease patients in the developing world die because they cannot afford renal replacement therapy—even when willing living kidney donors exist. This juxtaposition between countries with funds but no available kidneys and those with available kidneys but no funds, prompts us to propose an exchange program utilizing each nation's unique assets. Our proposal leverages the cost savings achieved through earlier transplantation over dialysis to fund the cost of kidney exchange between developed-world patient/donor pairs with immunological barriers and developing-world patient/donor pairs with financial barriers. By making developed-world healthcare available to impoverished patients in the developing world, we replace unethical transplant tourism with global kidney exchange—a modality equally benefitting rich and poor. We report the one-year experience of an initial Filipino pair, whose recipient was transplanted in the US with an American donor's kidney at no cost to him. The Filipino donor donated to an American in the US through a kidney exchange chain. Follow-up care and medications in the Philippines were supported by funds from the US. We show that the logistical obstacles in this approach, although considerable, are surmountable.

BO024 THE EVALUATION OF LONG-TERM RISK OF RENAL FAILURE FOR LIVING KIDNEY DONOR

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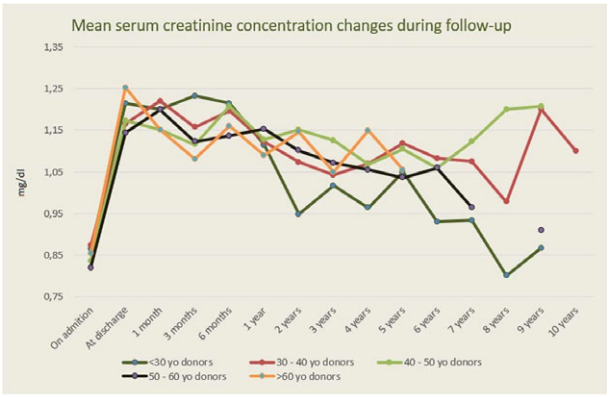
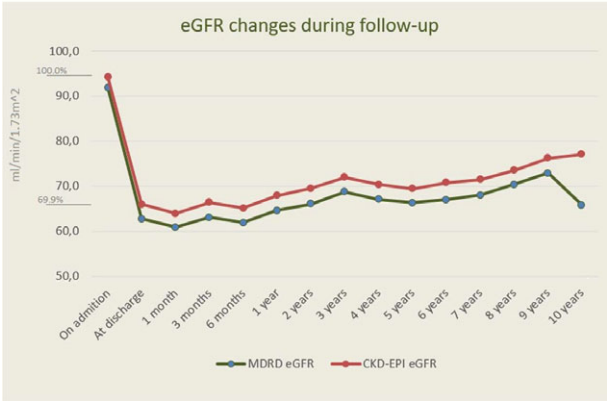
Background: Possibility of an increased risk of end-stage renal disease (ESRD) is a major concern related with living kidney donation. Monitoring of the remaining kidney function becomes the most important purpose of the follow-up system. Long-term safety of nephrectomy without accelerated loss of renal function is generally expected result.
Methods: Data analysis of 156 patients (aged 24–72) that underwent nephrectomy for organ donation in 2003–2016 was conducted. The efficacy of the long-term care system in the aspect of monitoring of the remaining kidney function was evaluated.
Results: Group consisted of 102 women and 54 men. Mean follow-up period was 5.44 years (range: 6 months – 10 years). The rise in value of mean serum creatinine concentration after donation was observed, but it was within the range of normal (0.6–1.3 mg/dl) during the observation. Results above laboratory testing standards (up to 2.2 mg/dl) were found in 26 cases. Mean postdonation GFR was measured at 68.3% of its predonation value with using MDRD formula and 69.99% when estimated with CKD-EPI. Despite of its initial declining after nephrectomy, mean GFR remained above 60 ml/min/1.73 m^2. MDRD GFR <45 ml/min/1.73 m^2 was observed only in 7 cases (4%), while MDRD GFR in the range of 45–60 ml/min/1.73 m^2 was found in 40 donors (23.3%). Only 21.5% of analyzed had CKD-EPI GFR estimated on 45–60 ml/min/1.73 m^2. It was found <45 ml/min/1.73 m^2 in 5 cases (2.9%), down to 33.7 ml/min/1.73 m^2. No one developed ESRD or required dialysis treatment.
Conclusions: Insightful qualification process minimizes the probability of being a kidney donor by someone with an increased risk of chronic kidney failure (CKF) in future. CKD-EPI formula seems to be more precise than MDRD for patients with higher levels of GFR and it should be used for kidney donors, as their loss of GFR is a result of nephrectomy, not kidney or systemic disease. Using MDRD formula may lead to inappropriate diagnosis of CKF in some cases.





BO025 INTEGRATION OF KIDNEY-EXCHANGE, (UN)SPECIFIED LIVING DONOR TRANSPLANTATION, ABO INCOMPATIBLE AND DESENSITISATION PROGRAMS IN A COMPUTERIZED ALLOCATION PROGRAM: A SIMULATION

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Background: Our kidney-exchange allocation program is established in 2004. Though kidney-exchange is intertwined with (un)specified donation and domino-paired procedures, the latter still operates by hand and on a local level. Desensitisation results are better for transplants with current negative but historically positive CDC crossmatches (CDC-XM) compared to current positive CDC-XM. An MFI<8000 is associated with negative CDC-XM. A computerised allocation program was developed to integrate these programs to increase efficiency and find matches with negative current CDC-XM for highly immunised (HI) patients (KEPmatch).
Methods: Our simulation included waitlisted patients, (un)specified donors and HLA- or ABO-incompatible (ABOi) pairs that participated in 2015. With

KEPmatch 4 runs were simulated with 3 months intervals. For HI patients (PRA > 85%) ABOi and MFI<8000 was allowed.
Results: In reality in 2015, 14 HI patients were included. There were 3 transplants via kidney-exchange program. Our matcher included 23 (un) specified donors haphazardly in time: 9 (un)specified donors initiated chains (7 with 1, 2 with 2 pairs), 14 donated to the waitlist. In total 37 transplants were carried out, none of the HI patients were matched. In the 4 KEPmatch runs respectively 6, 5, 5 and 7 (un)specified donors were included. 10 (un)specified donors were matched to the waitlist, 13 (un)specified donors initiated chains (9 with 1, 4 with 2 pairs). There were 2 kidney-exchange chains with 2 pairs, 1 chain with 3 pairs. KEPmatch found 44 matches: 20% more than in reality. On top of that 3 HLAi matches were found (anti donor MFI<8000) amongst 1 also ABOi. For these patients desensitisation is still indicated but success rate is high because of current negative CDC-XM.
Conclusion: Timing of inclusion and computer allocation to integrate programs leads to 20% more matches. Besides for 3 HLAi pairs matches were found that offered better chances in our desensitisation program.

BO026 A CLINICAL OUTCOMES IN RECIPIENTS OF LIVING DONOR KIDNEY TRANSPLANTS FROM ELDERLY DONORS: A SINGLE CENTER EXPERIENCE

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Background: Living donor kidney transplant (LDKT) accounts for more than 90% of all kidney transplants in Japan. LDKT donor guidelines define donors as healthy individuals aged 20–70 years. However, LDKT from elderly donors is debatable due to uncertainty in graft function. We evaluated the clinical outcomes of LDKT from elderly (≥60 years) donors.
Methods: From January 2008 to December 2015, 119 patients underwent LDKT at our center. We grouped them into elderly (ED; donors ≥60 years; $n = 41$) and normal donor groups (ND; donors <60 years; $n = 78$) and compared the outcomes.
Results: Donor age in ED and ND groups was 65.6 ± 4.1 and 46.5 ± 9.9 years, respectively. ED vs. ND preoperative HbA1c (5.8 ± 0.4 vs. 5.6 ± 0.4 ml/min, $p = 0.002$), estimated glomerular filtration rates (76.7 ± 13.2 vs. 90.3 ± 18.0 ml/min, $p < 0.001$), and creatinine clearance (92.1 ± 17.3 vs. 110.5 ± 20.8 ml/min, $p < 0.001$), were significantly different between the 2 groups. There was no significant difference in the number of patients in ED vs. ND groups, who required medication for acute T-cell mediated rejection (10/41 [24.4%] vs. 9/78 [11.5%]) ($p = 0.112$) and for cytomegalovirus infections (10/41 [24.4%] vs. 12/78 [15.4%]) ($p = 0.320$) within 1 year after LDKT. Serum creatinine levels, 3 years after LDKT, were significantly higher in the ED than in the ND group, but in the 4th year after LDKT there was no significant difference (ED vs. ND at 3 years: 1.63 ± 0.46 vs. 1.35 ± 0.66; $p = 0.012$; at 4 years: 1.50 ± 0.39 vs. 1.37 ± 0.60; $p = 0.213$). ED vs. ND graft survival rate and patient mortality rate after 5 years of LDKT (97.4 vs. 88.8%, $p = 0.400$) and (94.6 vs. 93.1%, $p = 0.694$) were not significantly different.
Conclusion: LDKT from elderly donors was found to be safe. Lower renal function was seen in the ED group in early years after LDKT; however, serum creatinine levels at 4 years were almost comparable. Careful selection of elderly donors and regular follow-up can achieve successful transplant outcomes.

BO027 THE INVESTIGATION AND OUTCOME OF LIVING KIDNEY DONORS WITH NON-VISIBLE HAEMATURIA: A 6-YEAR SINGLE CENTRE EXPERIENCE

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Background: Investigation of non-visible haematuria (NVH) in potential living kidney donors can include diagnostic flexible cystoscopy and/or renal biopsy. Counselling of potential donors with thin basement membrane disease (TBMD) on their renal biopsy, and the use of such patients as donors remains controversial.
Methods: We collected data for all potential donors in our centre from 2010 to 2015. (NVH) was defined as having urine dipstick positive for blood (including trace) on at least 2 occasions in the absence of infection. Investigations were performed as per BTS guidelines. Patients were divided into 3 groups: Group 1- potential donors with NVH who did not proceed to donation; Group 2 – patients with NVH who proceeded to donation; Group 3 (control group)- age, gender and race-matched donors without NVH. Post-donation estimated glomerular filtration rate (eGFR), blood pressure (BP) and presence/absence of proteinuria were compared between groups 2 and 3.
Results: Between 2010 and 2015 we screened 886 potential living kidney donors, and 69/886 (7.8%) were found to have NVH. 54/69 (78.2%) patients with NVH did not proceed to donation (group 1). 21/69 (30.4%) patients with NVH had renal biopsies, showing TBMD in 16/21, no pathology in 4/21 and a new diagnosis of IgA nephropathy in 1/21 patients. No complications occurred following renal biopsy. Of the patients with TBMD, 7/15 proceeded to donation. 4 patients with TBMD underwent genetic testing, which was positive in one patient (COL4A3 G871C mutation). No significant difference in eGFR, BP and proteinuria was identified between groups 2 and 3 at a mean follow-up of 2.8 years.
Conclusion: (NVH) is a common finding amongst potential living kidney donors in our institution, but only a minority of patients proceed to donation. TBMD is the commonest finding in potential donors who undergo a renal biopsy, but the role of genetic testing in these patients needs to be better defined, as does their suitability as living kidney donors.

Basic Kidney Donation and donor types

BO028 IMPACT OF THE POST-TRANSPLANT RECIPIENT'S EVOLUTION IN THE QUALITY OF LIFE OF LIVING KIDNEY DONORS

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Introduction: Studies on the post-donation outcome of Living kidney Donors (LKD) are usually orientated to the medical consequence of organ donation. However, there is a very few data that evaluating the impact on how the recipient medical evolution and post-transplant complications can impact the LKD's Quality of Life (QoL).
Objective: To determine the impact of post-transplant recipient's evolution in the QoL of LKD evaluated in the tertiary level and University Hospital.
Methodology: A follow-up at list one year after kidney living donation was applied to all LKD between the years 1999–2014. We used three selected ad hoc psychosocial validated questions from European Living Donor Psychosocial Follow-up (ELIPSY project) to assess the perception of the LKD about recipient's outcome: 1-The recipient status (alive or not); 2-The LKD perception about their recipient health status; 3-The LKD perception about their recipient behaves in a way that risks the continued healthy functioning of the graft. These questions were linked with their QoL using the SF-36 questionnaire. LKD were contacted by phone to inform about the study and request their inform consent. If LKD approved the protocol was sent by mail post and to be returned. For the statistical analysis independent T-test and Chi-square were performed.
Results: During the years of the study have been 514 LKD; 491 met the inclusion criteria; 417 give their consent to participate; and 350 LKD (72%) return the questionnaire. As a first analysis, the eight scales and two component scales (physical and mental) of SF-36 was calculated and 17 outliers LKD were found and were analyzed case be case and have been excluded. Mean T-scores of SF-36 were above 50 felling within the normal range compared to the general population in all scales. However, we were observed that mental component summary score was lower if the recipient died ($p = 0.003$) and also if the LKD has the perception that their recipient health is bad ($p = 0$).

Translational Kidney Biomarkers and molecular changes

BO029 PROSPECTIVE MATCHED CONTROL EXPLORATION OF CHEMOKINES UNDER BELATACEPT THERAPY COMPARED TO CONVENTIONAL IMMUNOSUPPRESSION WITH CNI AND MTORI

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Only limiting data exist concerning chemokine profile of patients (pts) under belatacept (BEL) based therapy after renal transplantation (tx).

The evaluation of certain chemokines may offer an opportunity to explore the effect and the impact of different immunosuppressive regimen.

$N = 20$ pts were converted from a calcineurin inhibitor (CNI) or inhibitor of mammalian target of rapamycin (mTORi) to a BEL-based regimen compared to control pts ($n = 20$, matched for age, sex, and renal function) with continued CNI or mTORi therapy.

Bel was administered 5 mg/kg at day 0, 14, 28, 42, 56, every 4 weeks. Plasma samples were collected for baseline (BL), Month (Mo) 1 and Mo3. 23 Chemokines (in particular CCL1, CCL15, CCL17 and CXCL12) were analyzed by the Luminex-based multiplex technique and calculated as absolute values (pg/nl).

After conversion to Bel only pts that were converted from CNI express higher levels of CCL1 (BL: 6.98 vs. M3: 8.77; $p = 0.046$). CCL15 showed an increase in pts that were converted from only mTORi to BEL (BL: 6290.8 vs. M3: 6459.7; $p = 0.011$). Pretreatment with CNI had no effect on CCL15. Interestingly, levels of CCL17 were lower already 1 M after conversion from CNI to BEL (BL: 131.2 vs. M1: 97.1; $p = 0.037$). CXCL12 expression increases significantly under BEL treatment in mTORi converted pts (BL: 2872.7 vs. M3:

3218.7; p = 0.021). Control pts showed in each expression profile no significant changes between BL and each investigation time point.

Interestingly, after conversion from CNI to Bel there were higher levels of CCL1 and lower levels of CCL17, that reflect a more pro inflammatory condition via CCR8 and a lower chemotactic conditions via CCR4 for T-cells. After conversion from mTORi to Bel there were higher levels of CCL15 and CXCL12 that lead to a more pro inflammatory condition with activation of T- and antigen presenting cells. In summary, Bel shift chemokine environment to a more inflammatory phenotype.

Basic Kidney Biomarkers and molecular changes

BO030 COMPARATIVE STUDY ON THE ISOLATION OF URINARY EXOSOMES USING DIFFERENT METHODS TO DISCOVER NOVEL KIDNEY REJECTION BIOMARKERS

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Background: Rapid and accurate diagnosis of renal allograft injury by renal biopsy could lead to prompt treatment improving graft survival. In this perspective, the identification of reliable non-invasive biomarkers for allograft injury could allow earlier monitoring. Urinary exosomes (UExs), lipid membrane-bound nanovesicles (40–150 nm of diameter) released also from the kidney cells are, for instance, a useful noninvasive predictive biomarkers of rejection. Different studies demonstrated that UExs carry different types of cargo (e.g. miRNA, proteins) and reflect the physiological status of the cells they originated from. However, due to their low amount, UExs concentration and characterization remain a challenge. This study aims to identify the most efficient UExs isolation method both for RNA profiling and proteomic analysis to discover novel renal transplant rejection biomarkers.
Methods: UExs were isolated from 5 ml filtered urine using 3 different commercial kits (Norgen, ExoQuick and Qiagen), compared to the ultrafiltration method. UExs were quantified by qNano instrument. Chromatography column kit was used to extract total RNA, included small RNA species and biochemical assay was used to extract proteins. miRNA and protein integrity and concentration were evaluated by Agilent Bioanalyzer 2100.
Results: The comparison among the 4 methods highlighted a high variability in the raw concentration of UExs (3.5×10^8–3.5×10^{12}) and showed different UExs size (90–130 nm). qNano reports indicated that Qiagen kit was the most efficient isolation method for UExs. However, Agilent Bioanalyzer RNA analysis emphasized that the highest amount of miRNAs was obtained using Norgen Kit. Same kind of experiments are currently undergoing for the UExs proteins content.
Conclusions: All four methods yielded UExs, although a great variability in the UExs number and diameter was observed. Based on our results, the most efficient method for miRNA UExs isolation is Norgen kit.

Clinical Kidney Biomarkers and molecular changes

BO031 SCLEROSTIN IS NOT ASSOCIATED WITH CARDIOVASCULAR EVENTS IN KIDNEY TRANSPLANTATION CANDIDATES

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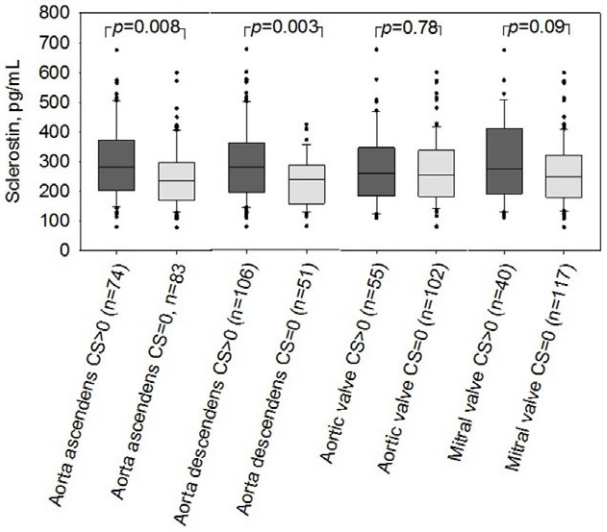
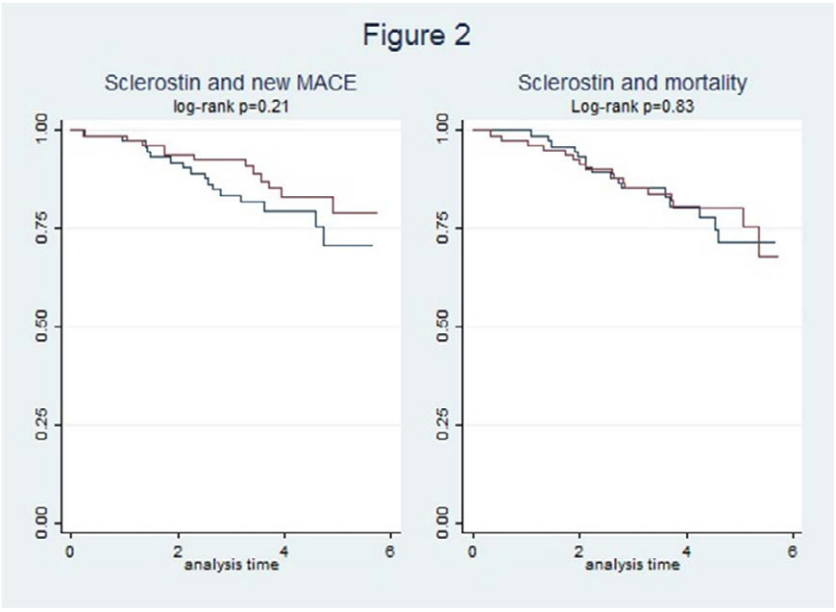
Background: Sclerostin, a bone derived protein, has been linked to cardiovascular calcifications. This study investigated the associations between sclerostin and bone and cardiovascular disease in kidney transplant candidates.

Figure 1 Sclerostin and vascular calcification in kidney transplant candidates





Methods: Cardiac computed tomography scans were performed in 157 kidney transplant candidates. Calcification scores (CS) were calculated for coronary arteries (CA), ascending aorta (AA), descending aorta (DA), aortic valve (AoV) and mitral valve (MiV). Bone mineral density (BMD) was measured at lumbar spine and total hip. Blood samples were drawn in the fasting state and Sclerostin was analysed by ELISA (R&D). Events were registered through review of patient records until 31.10.2016.
Results: Median age was 54 (range 32–72) yrs and 68% were men. Patients on dialysis (n = 59, 62%) had 21% higher levels of sclerostin compared to pre-dialysis patients (CI 9–32%, p = 0.001). Sclerostin was positively correlated with age (r = 0.32, p < 0.001), BMI (r = 0.26, p = 0.001) and Z-scores of lumbar spine (r = 0.21, p = 0.01) and total hip (r = 0.53, p > 0.001).

Higher levels of sclerostin were seen in patients with vascular calcifications (Figure 1). Sclerostin was a positive predictor independent of age and sex of CACS (β=0.005, p = 0.02) and BMD of spine (β=21.7, p = 0.002) and hip (β=39.3, p < 0.001). During a median follow-up of 4.3 years (range 3.1–5.8), 34 patients died, 29 had a major cardiovascular event (MACE) and 19 had a fragility fracture. Sclerostin levels above/below median did not predict all-cause mortality or MACE (Figure 2) or fragility fracture (p = 0.65). Sclerostin as a continuous variable was not associated with risk of events (p = 0.70, 0.70 and 0.60, respectively).
Conclusions: Sclerostin levels are positively associated with bone density and vascular calcification in kidney transplant candidates; but this does not appear to translate into a predictive ability of future events related to chronic kidney disease mineral and bone disorder.

BO032 IGG HYPOGAMMAGLOBULINEMIA: A RISK FACTOR OF CMV INFECTION IN A MULTICENTER STUDY IN KIDNEY TRANSPLANTATION

Elizabeth Sarmiento[1], Maria Luisa Rodriguez-Ferrero[1], Marcos Lopez-Hoyos[2], Boris Karanovic[3], Manuel Arias[2], Emilio Rodrigo[2], Fernando Anaya[1], Patricia Muñoz[1], Alia Eworo[1], Joaquin Navarro[1], Pilar Catalan[1], Javier Carbone[4]
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Background: IgG hypogammaglobulinemia has been demonstrated as a risk factor of severe infection in solid organ transplantation in single center studies and metanalysis. Kidney transplant patients are more prone to CMV infection due to immunosuppressive therapy. We here present the results of a multicenter study with the aim to evaluate distinct humoral immunity biomarkers as potential predictors of CMV infection.
Methods/Materials: In a prospective multicenter study of a cohort of 212 patients in 2 centers in Spain who underwent kidney transplantation we identified patients who developed CMV infection during a 6 month follow-up after transplantation. Levels of IgG, IgM, IgA and complement C3 and C4 were prospectively measured in both centers using the routine laboratory. Assessment times were before transplantation, at day 7 and at day 30 after transplantation. Logistic regression analysis was performed to assess potential biomarkers.
Results: During follow up 18 (8.5%) kidney recipients developed at least one episode of CMV infection. Day 30 IgG level was lower in patients who developed CMV infections after transplantation compared to patients without this complication (704 ± 276 and 894 ± 281%, respectively, p = 0.013). IgG level <750 mg/dl (IgG hypogammaglobulinemia) was significantly associated with risk for development of CMV infection in logistic regression analysis, RH 5.89, 95% CI 1.79–19.44, p = 0.004. Patients with hypogammaglobulinemia also disclosed a higher risk of developing recurrent infections (defined as 3 or more episodes caused by distinct pathogens, 24.1%), RH 2.4, 95% CI, 1.12–4.95, p = 0.024).
Conclusion: The results obtained in this multicenter study suggest that lower levels of IgG are a risk factor for development of CMV infection in kidney transplantation. IgG assessment is easily available, rapid and low cost. The inclusion of this biomarker in immunomonitoring protocols should be taken into account.

BO033 A RAPID AND SUSTAINED IMPROVEMENT OF CALCIFICATION PROPENSITY SCORE (SERUM T50) AFTER SUCCESSFUL KIDNEY TRANSPLANTATION: RE-ANALYSIS OF A RANDOMISED CONTROLLED CLINICAL TRIAL OF IBANDRONATE

Knut Smerud[1], Anders Åsberg[2], Håkon Kile[1], Andreas Pasch[3], Dag Olav Dahle[2], Jens Bollerslev[4], Kristin Godang[5], Anders Hartmann[2]
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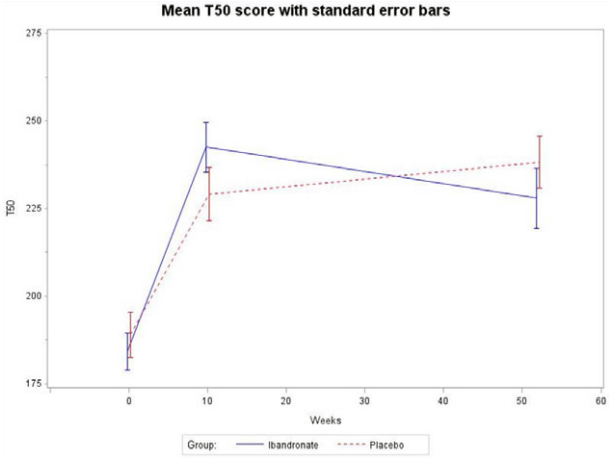
Background: A serum test called T_{50} assesses the overall propensity for calcification of blood and is associated with cardiovascular outcomes. We aimed to examine T_{50} over time in kidney transplant recipients and also address any effects of ibandronate.
Methods/Materials: Serum samples taken from kidney transplant patients included in a 1-year prospective, randomized placebo controlled study of ibandronate were analyzed in retrospect. All patients received underlying supplementation with calcium and active vitamin D_3. Study baseline was within four weeks after transplantation, when a clinically stable and adequate graft function (estimated glomerular filtration rate > 30 ml/min/1.73 m^2) had been obtained. Serum T_{50} analyses were performed at baseline in 129 patients, at 10 weeks in 127 patients and at one year in 123 patients.
Results: Ibandronate caused no differences to placebo in T_{50} at 10 weeks (p = 0.094) or at 1 year (p = 0.116). Baseline T_{50} was a significant covariate (p < 0.0001) for T_{50} scores at 10 weeks and 1 year. In the total cohort there was a highly significant (p < 0.0001) increase in T50 of 26.6% after 10 weeks and T_{50} remained stable after one year. For change in T_{50}, there was an inverse correlation to phosphate of −0.515 (p < 0.0001) and to change in serum albumin (p < 0.03).
Conclusion: T_{50} increased from baseline to 10 weeks after transplantation with no further change after one year. Ibandronate had no effect on T_{50} compared with placebo. The significantly improved calcification propensity measured with the T_{50} score is encouraging in terms of utilizing this variable as a potential early biomarker for improved prognosis of cardiovascular mortality in the kidney transplant setting.



BO034 SOLUBLE TIM-3 IS ASSOCIATED WITH RENAL FUNCTION IN RENAL TRANSPLANT RECIPIENTS

Ya-Mei Li[1], Yi Li[1], Yun-Ying Shi[2], Yang-Juan Bai[1], Xiao-Juan Wu[1], Bei Cai[1], Lan-Lan Wang[1]
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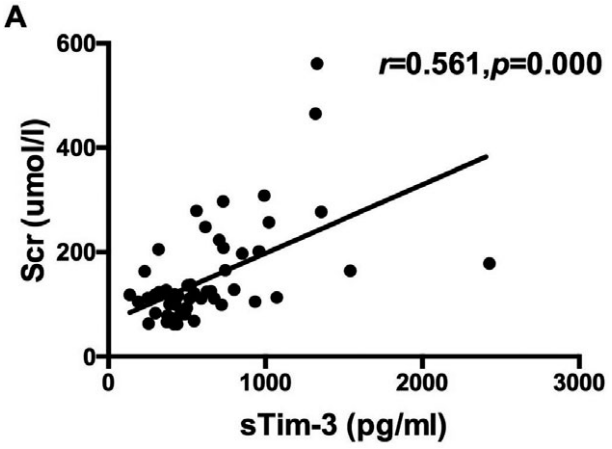
Background: Chronic renal allograft rejection remains a major hurdle that affects the long-term survival of renal allografts. Finding novel noninvasive biomarkers of chronic allograft rejection is of great benefit for patients and graft outcomes. T-cell immunoglobulin domain and mucin domain-3 (Tim-3) has been identified as a co-inhibitory molecule, participating in the regulation of immune response and the induction of allograft tolerance. Here we explored the association of cellular Tim-3 (cTim-3) and soluble Tim-3 (sTim-3) with the renal

function of renal transplant recipients (RTs). Moreover, the application of cTim-3 and sTim-3 in diagnosing chronic allograft rejection were further evaluated among RTs.
Methods: Periphery whole blood and serum samples were collected from 58 RTs, including 27 with impaired renal function planning for allograft needle biopsy (10 recipients were classified as having chronic allograft rejection after allograft biopsy) and 31 with stable renal function. Surface expressions of Tim-3 on CD4 + and CD8 + T cells were determined by flow cytometry. sTim-3 was quantified by Enzyme-linked immunosorbent assay (ELISA).
Results: The level of sTim-3 was significantly and positively correlated to serum creatinine (Scr) levels (Fig. A), while the expressions of cTim-3 were not associated with Scr levels. The area under receiver-operating curve (ROC) for sTim-3 to diagnose chronic allograft rejection was 0.810 (95% CI, 0.704–0.916, p = 0.005) with an optimal cut-off level of 603.8 pg/ml, which would achieve a 100% sensitivity and a 72% specificity. However, cTim-3 showed no such ability to diagnose chronic allograft rejection in RTs.
Conclusions: Our data indicated that soluble Tim-3, instead of cellular Tim-3, was a novel marker reflecting renal function in RTs. Moreover, soluble Tim-3 might be a promising noninvasive biomarker for chronic allograft rejection diagnosis.



Translational Kidney Biomarkers and molecular changes

BO035

FP7 BIOMARGIN SHOWS THAT A SMALL SET OF BLOOD MICRO-RNAS IS ASSOCIATED WITH ACUTE KIDNEY ALLOGRAFTS REJECTION

Claire Tinel[1], Aurélien Benon[1], Stéphane Gazut[2], Maarten Naesens[3], Wilfried Gwinner[4], Marie Essig[5], Pierre Marquet[6], Dany Anglicheau[1]
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Background: FP7 Biomargin aimed at detecting and validating non-invasive biomarkers of kidney graft lesions. After untargeted screening of different –omics, candidate biomarkers were confirmed in independent patient groups. In this study, we investigated the diagnostic potential of microRNAs (miRNAs) in whole blood samples.
Methods/Materials: Blood samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Biopsies were retrospectively selected after centralized histological reading by expert pathologists, and classified into 4 groups (Normal, ABMR, TCMR or IF/TA), to build two independent case-control studies (discovery- and validation sets). Global microRNA (miRNAs) profiling was performed on blood samples from the discovery set by TaqMan® Array microRNA v3 microfluidic cards (TLDA, Life Technologies). A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify a list of biomarker candidates associated with one of the 4 groups. This list of miRNAs was quantified using custom TLDA plates on the validation set. Multivariate models were then built to define miRNAs signature of graft lesions.
Results: A total of 754 miRNAs was quantified in the discovery set that included 42 Normal, 17 TCMR, 37 IF/TA and 30 ABMR samples. Our statistical pipeline identified 141 candidates that were assessed in the validation cohort of 37 Normal, 23 TCMR, 41 IF/TA and 37 ABMR samples. The table shows the association between histological phenotypes and miR-derived statistical models in the validation cohort.

Group comparison	Number of miRNAs in the best model	Mean AUC*
Rejection vs. Normal	4	0.70
TCMR vs. Normal	6	0.75
ABMR vs. Normal	4	0.81
ABMR vs. TCMR	5	0.64
ABMR vs. IF/TA	5	0.72

*Estimated by resampling approaches.
Conclusion: We identified a small subset of miRNAs in the blood with a strong association with ABMR and/or TCMR, thus providing the basis for innovative non-invasive molecular tools development. Their diagnostic performance is currently being investigated in blood samples collected at time of 453 consecutive allograft biopsies in our BIOMARGIN trans-sectional study.

Translational Liver Biomarkers and molecular changes

BO036

A GLYCOMIC BASED SERUM MARKER ANALYSED ON POSTOPERATIVE DAY 7 AFTER LIVER TRANSPLANTATION IS AN INDEPENDENT PREDICTOR OF GRAFT AND PATIENT SURVIVAL DURING THE FIRST YEAR AFTER LIVER TRANSPLANTATION

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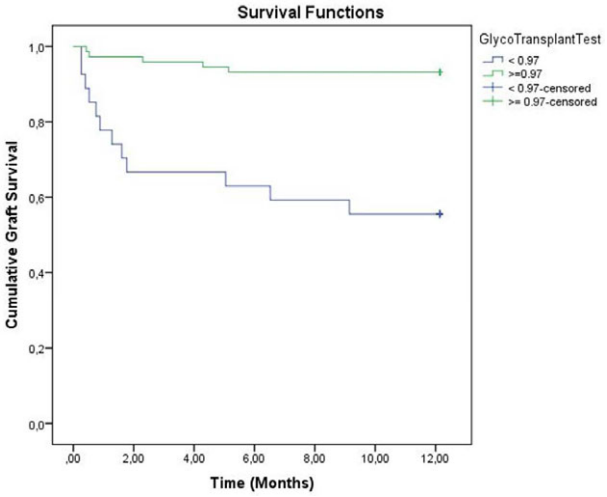
[1]Ghent University Hospital, Belgium; [2]Medical Biotechnology Center Vib, Belgium

Background and Aims: Poor graft function after liver transplantation (LT) remains a challenge and can lead to retransplantation. Biomarkers that reliably identify patients at risk for graft failure after LT are lacking. Analysis of N-glycans in serum (glycomics) has shown to reflect the underlying liver function in liver disease but has never been assessed after LT. The aim of this study was to assess the potential of serum glycomics as predictive markers for graft and patient survival after LT.
Methods: In this monocentric prospective cohort 127 liver transplant patients were included between 1 December 2012 and 31 December 2014. Serum samples were collected just before and on daily bases during the first 2 weeks after liver transplantation. Glycomic profiles were analysed using an optimized glycomic technology on a DNA sequencer. The major outcome parameters (graft and patient survival during 1 year) were related to the observed glycomic alterations and the best predictive association was searched for using cox regression analysis.
Results: The assessment of 2 serum glycans NG1A2F (an agalacto, core-alpha-1,6-fucosylated biantennary glycan structure) and NA3 (a triantennary glycan), combined as log(NG1A2F/NA3) on day 7 after LT was strongly associated with graft loss (hazard ratio = 7.222; p < 0.001; 95% CI 2.352–22.182) and patient death (hazard ratio = 3.885; p = 0.30; 95% CI 1.127–13.276) during the first year after LT (cox regression analysis). In a multivariable cox regression model including early allograft dysfunction (according to Olthoff) and Donor Risk Index, this glycomic marker, called GlycoTransplantTest, was the only independent predictor of graft survival (p = 0.003).



Conclusions: Assessment of GlycoTransplantTest, a glycomic serum marker, on day 7 post LT is a strong and independent predictor of graft and patient survival during the first year after LT. This glycomic marker can be analysed on routine clinical capillary electrophoresis equipment.

Clinical Kidney Biomarkers and molecular changes

BO037 A HIGH NUMBER OF REGULATORY T CELLS IN PERIPHERAL BLOOD AT 1 YEAR AFTER KIDNEY TRANSPLANTATION IS AN INDEPENDENT PREDICTOR OF LONG-TERM GRAFT SURVIVAL

Luis Humberto Galvan Espinoza[1], David San Segundo Arribas[2], Emilio Rodrigo Calabia[1], Juan Irure Ventura[2], Juan Carlos Ruiz San Millan[1], Gema Fernandez Fresnedo[1], Esther Asensio[2], Jairo Bada Da Silva[1], Lara Belmar[1], Marcos Lopez Hoyos[2]

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Background: Progressive reduction in acute rejection rates has led to an improvement of kidney graft survival throughout the first year, but long-term graft attrition rates remain stable beyond this point. It is known that regulatory T cells (Tregs) play a role in limiting kidney transplant rejection and can potentially promote long-term transplant tolerance. Despite this, there are no large studies that demonstrate the role of peripheral blood Tregs on long-term graft outcome. The aim of our study was to analyze the influence of 1-year peripheral blood Tregs on long-term death censored graft survival.
Methods/Materials: A total of 133 consecutive kidney transplant recipients between 2005 and 2011 were included in the study. Tregs were measured prospectively and identified as $CD4^+CD25^{high}Foxp3^+$ and/or $CD4^+CD25^+CD127^{low}Foxp3^+$ by flow cytometry Death censored graft survival was assessed in January-2017.
Results: Mean follow-up was 7.4 ± 2.9 years and 32 (24.1%) patients suffered death censored graft loss (DCGL). One-year peripheral Tregs were 17.4 ± 16.9 cells/mm^3. Patients with high Tregs above the median value (13.0 cells/mm^3) showed better death-censored graft survival (5-year 92.5% vs. 81.4%, Log-rank p = 0.030). One-year Tregs showed AUC-ROC of 63.1% (95% CI 52.9–73.2%, p = 0.026) for predicting DCGL. After multivariable Cox's regression analysis, a high number of peripheral blood Tregs was a protective factor for DCGL (HR 0.961, 95% CI 0.924–0.998, p = 0.041) independent of 1-year proteinuria and renal function.
Conclusion: A high number of peripheral blood Tregs at 1-year after kidney transplantation relates to a better long-term graft outcome. This relationship was independent of other significant 1-year variables. In this sense, peripheral blood Tregs can be useful as a biomarker to predict graft outcomes and to tailor immunosuppression.

Translational Kidney Biomarkers and molecular changes

BO038 FP7 BIOMARGIN SHOWS THAT SMALL SETS OF INTRA-GRAFT MICRORNAS ARE STRONGLY ASSOCIATED WITH RENAL ALLOGRAFT LESIONS

Claire Tinel[1], Aurélien Benon[1], Stéphane Gazut[2], Maarten Naesens[3], Wilfried Gwinner[4], Marie Essig[5], Pierre Marquet[6], Dany Anglicheau[1]

[1]Necker Hospital, France; [2]Cea, France; [3]Ku Leuven, Belgium; [4]Mh Hannover, Germany; [5]Limoges University Hospital, France; [6]Limoges University, France

Background: FP7 Biomargin aimed at detecting and validating biomarkers of kidney graft lesions. After untargeted screening of different –omics, candidate biomarkers were confirmed in independent patient groups. In this study, we investigated the diagnostic potential of microRNAs (miRNAs) in allograft biopsy samples.
Methods/Materials: Biopsies were collected from protocol or for-cause biopsies in 4 European clinical centers. Samples were retrospectively selected after centralized histological reading by expert pathologists, and classified into 4 groups (Normal, ABMR, TCMR or IF/TA), to build two independent case-control studies (discovery- and validation sets). Global miRNA profiling was performed on TaqMan® Array microRNA v3 microfluidic cards (TLDA, Life Technologies) on the discovery set. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify an extended list of biomarker candidates associated with one of the 4 groups. This extended list of miRNAs was quantified using custom TLDA plates on the validation set. Multivariate models were then built to define miRNA signatures of graft lesions.
Results: A total of 754 miRNAs was quantified in the discovery set that included 32 Normal, 13 TCMR, 25 IF/TA and 18 ABMR samples. Our statistical pipeline identified 140 candidates that were assessed in the validation cohort of 32 Normal, 13 TCMR, 26 IF/TA and 28 ABMR samples. The table shows the association between histological phenotypes and miRNA-derived statistical models in the validation cohort.

Group comparison	Number of miRNAs in the best model	Mean AUC*
ABMR vs. Normal	4	0.76
ABMR vs. TCMR	3	0.90
ABMR vs. IF/TA	6	0.94
TCMR vs. Normal	6	0.96
Rejection vs. Normal	3	0.95
Rejection vs. No Rejection	4	0.86

*Estimated by resampling approaches.
Conclusion: We identified a small set of miRNAs within kidney allograft biopsies with a strong association with TCMR and ABMR. These miRNA signatures might provide useful molecular tools to improve allograft assessment. Their diagnostic performance is currently being investigated in our BIOMARGIN trans-sectional study of 312 consecutive allograft samples.

Basic Kidney Biomarkers and molecular changes

BO039 CELL-FREE MICRORNAS IN KIDNEY GRAFT PRESERVATION FLUID AS NOVEL BIOMARKERS FOR DELAYED GRAFT FUNCTION

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[1]Erasmus Medical Center - Department of Surgery, The Netherlands; [2]Erasmus Medical Center - Department of Pathology, The Netherlands

Background: Delayed graft function is a common complication after deceased donor kidney transplantation (KT), which affects both short and long-term outcome. Currently available biomarkers in graft preservation fluid lack sensitivity in predicting outcome after transplantation. The aim of this study is to identify microRNAs in preservation fluid predictive of delayed graft function (DGF) after transplantation.
Methods: In this study, preservation samples were collected during kidney transplantations from deceased donors. The graft outcome was defined as DGF or immediate graft function (IF). As a discovery cohort, 4 IF samples and 4 DGF samples were analysed using TaqMan Array MicroRNA cards with 2 grafts from both DCD (donation after cardiac death) and DBD (donation after brain death) in each group. As validation cohort, we analysed 40 IF and DGF samples.
Results: On average, 222 miRNAs (range 192–246) were detected per sample with 223 miRNAs fulfilling the pre-set parameters (Ct<40 in 3 or more samples). PCR array expression analysis using the HTqPCR package for R returned 7 miRNAs with p < 0.01. After correcting for multiple testing only miR-505 remained significantly different between the groups (p = 0.02). We confirmed this in an independent validation cohort using regular miRNA qPCR assays (p = 0.0071). If samples were stratified for donor type, miR-505 remained significantly different between IF and DGF in DCD kidneys.
Discussion: MiRNAs in graft preservation fluids are well detectable and can be a promising source for biomarkers of graft quality and for predicting outcome prior to kidney transplantation. In the era of extended criteria donor organs, this may have great clinical impact for graft reconditioning strategies to improve transplant outcome.

Clinical Others Other

BO040 NEUTROPENIA IN KIDNEY AND LIVER TRANSPLANT RECIPIENTS: RISK FACTORS AND OUTCOMES

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Aim: This study aimed to: 1) Define the risk factors associated with neutropenia within the first-year post kidney or liver transplantation; 2) Describe

the association between neutropenia and patient survival, infection, or acute rejection.
Methods: In this single-center, retrospective, cohort study, we enrolled all adult patients who received a kidney (KTx) or liver transplantation (LTx) between 2000 and 2011. Neutropenia was defined as two consecutive absolute neutrophil count (ANC) values lower than 1500/mm^3. The first neutropenia episode occurring during the first-year posttransplantation was analyzed. Patients with preexisting neutropenia were excluded. Median follow-up was 55 months.
Results: 663 patients with KTx and 354 patients with LTx met the inclusion criteria. The incidence of neutropenia was 20% in KTx, and 38% in LTx, and the median time to onset of neutropenia was 91 and 78 days, respectively. The median lowest ANC was 790 in KTx, and 900/mm^3 in LTx, and the median duration of each episode was 14 days in both groups. High-risk CMV status and valganciclovir (VGCV) use were significant predictors of neutropenia for KTx recipients, but only VGCV use vs. non-use in LTx recipients. Neutropenia was associated with worse survival in KTx recipients (adjusted HR 1.95, 95% CI 1.18–3.22, $p < 0.01$), but not in LTx recipients (adjusted HR 0.75, 95% CI 0.52–1.10, $p = 0.15$). Sixteen acute rejection episodes were associated with preceding neutropenia in KTx recipients (HR 1.77, 95% CI 1.16–2.68, $p = 0.007$), but only two of them led to graft loss. Twenty-four acute rejection episodes were associated with preceding neutropenia in LTx recipients (HR 1.41, 95% CI 0.97–2.04, $p = 0.07$), but only one led to graft loss. The incidence of infection was similar in patients with and without neutropenia among KTx and LTx recipients.
Conclusion: Neutropenia is associated with worse patient survival, and higher acute rejection rates in KTx recipients, but not in LTx recipients.

Clinical Kidney Immunology

BO041 THE BALANCE BETWEEN INTERLEUKIN 17-SECRETING T HELPER CELLS AND REGULATORY T CELLS AFTER RENAL TRANSPLANTATION: RELATION TO GRAFT FUNCTION AND SURVIVAL

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Background: T helper (Th) 17 cells, a subset of Th cells, are major mediators of inflammation-associated disease and have a reciprocal developmental relationship with the immunosuppressive regulatory T (Treg) cells, which actively restrain the inflammatory response. Th 17 has the exclusive ability to produce interleukin (IL)-17A.
Methods/Materials: This study included 60 subjects; they were divided into three groups each 20, renal transplant patients with stable renal function (Group I), with chronic allograft dysfunction (CAD) (Group II) and healthy subjects as controls (Group III). The Th cells, Th17 cells and Treg cells in fresh whole blood samples were identified as CD3 + CD4 + , CD4 + IL17 + and CD4 + CD25 + FoxP3 + cells respectively using flow cytometry and expressed as percentages of total lymphocytes. Serum and urinary IL17A levels were measured using solid phase sandwich enzyme linked immunosorbent assay (ELISA) kit. Renal hemodynamics was evaluated by duplex Doppler ultrasonography and resistive and pulsatility indices (RI, PI) were calculated.
Results: Renal transplant recipients, especially patients with CAD, showed significant increases in the percentage of Th17 cells, total CD4 + Th cells, Th17/FoxP3 + Treg ratio, serum and urinary IL17 levels and a significant decrease in the percentage of circulating FoxP3 + Treg cells compared with healthy subjects ($p < 0.01$). The percentage of Th17 cells were positively correlated with serum and urinary IL17, Th17/FoxP3 + Treg ratio, and inversely correlated with the percentage of circulating FoxP3 + Treg cells ($p < 0.01$). The increased of RI and PI were positively correlated with renal function and cyclosporine trough level.
Conclusions: In renal transplant recipients the CD4 + Th cell phenotype is skewed toward the IL17 producing cells with the increase of serum IL 17. The imbalance between Th17 and Foxp3 + Treg cells plays an important role in graft dysfunction with deterioration of renal function.

BO042 IMPACT OF CYTOKINE GENE POLYMORPHISM ON CLINICAL OUTCOME OF RENAL TRANSPLANTATION

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Background: Cytokine production is subject to genetic regulation, in such a way that gene polymorphisms at the level of promoter or coding regions can alter their levels and modify the immunologic response. We evaluate the influence of single nucleotide polymorphisms (SNPs) of IL10, TNFα, IFNγ and IL18 on early renal graft outcomes.
Methods: Observational study that included 709 consecutive patients who received a first renal transplant at our center from 2005 to 2011. SNP analysis was carried out by real-time PCR using TaqMan® probes. Patients were stratified according to the higher production genotype. A control group that included healthy subjects was used to confirm that the genotypic data obtained conformed to the expected frequencies in accordance with the Hardy-Weinberg equilibrium.
Results: There was a significant association between SNP of TNFα-308G/A and acute vascular rejection (AVR) in the adjusted logistic regression model. Allele A carriers had nearly a threefold higher risk of developing AVR (OR=2.64; CI 95%: 1.46–4.76; $p = 0.001$) compared to those who had GG genotype. In the analysis for risk of delayed graft function (DGF), stratified according to donor type, an association between DGF and SNP of TNFα-308G/A in grafts from donors after brain death (DBD) was found. A further association was observed between DGF and SNP of IL18-137 G/C in grafts from donors after cardiac death (DCD). Regarding renal graft recipients from DBD, TNFαGA/AA genotypes had a higher risk of DGF (OR=6.15; CI 95%: 1.65–22.86; $p = 0.007$); while in those from DCD, G allele carriers within SNP-137G/C of IL18 had the higher risk (OR=2.76; CI 95%: 1.03–7.40; $p = 0.042$).
Conclusions: SNP-308G/A of TNFα can be considered as a non-invasive risk biomarker for AVR and, in grafts coming from DBD, DGF. On the other hand, SNP-137G/C of IL18 was the main genetic marker for DGF in grafts from DCD. The knowledge of these polymorphisms previous to transplantation could aid in individualizing immunosuppression.

Translational Others Cancer

BO043 NEOPLASTIC RISK DONORS IN THE EMILIA-ROMAGNA REGION: THE TIMES THEY ARE A-CHANGIN'

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Introduction: The "Neoplastic Risk Donor" protocol was implemented in Italy in 2003. This protocol is uniform nationwide and provides organ donation from donors presenting either present or past history of neoplasia: donation is allowed for some kind of malignant tumour after evaluation of its grading, staging and tumour free interval prior to donation. Organs of this kind of donors are allocated to a very selected recipients category. Uniform informed consent and monitoring follow-up programme are provided to the recipients. The National Second Opinion in Pathologic Anatomy supports this protocol. The protocol has been split into 2 levels ("Non Standard Minimal Risk" and "Non Standard Acceptable Risk") since October 2015. Aim of this study is to review "Neoplastic Risk Donor" organ procurement in the Emilia-Romagna region (ERR, Northern Italy region of 4 550 500 inhabitants) and related transplantations which were performed from 2006 to 2016.
Materials and Methods: All "Neoplastic Risk Utilized Donors" and all organs with related transplantations from the 1st of January 2006 to the 31st of December 2016 in the ERR were reviewed.
Results: 56 neoplastic risk utilized organ donors with 110 organs in all (55 livers, 38 kidneys, 10 lungs, 6 hearts and 1 pancreas) were reported between the 1st of January 2006 and the 31st of December 2016. The percentage of these donors on total utilized donors in the same period is 3.8%. The most frequently affected organs were: Kidney and Central Nervous System (24%), Prostate (14.7%), Skin (12%), Uterus (8%). In this period 90 transplants were carried out, 57 of them between 2014 and 2016. Data concerning recipient survival still have not reported neoplasia transmission.
Conclusion: "Neoplastic Risk Donors" are more and more increasing, due to the high age average of deceased potential donors; low risk of neoplasia transmission between donor and recipient seems to emerge by this study, provided that the dedicated.

Clinical Kidney Cancer

BO044 PRE-TRANSPLANT MALIGNANCY ON KIDNEY TRANSPLANT RECIPIENTS IS NOT ASSOCIATED TO THE INCIDENCE OF POST-TRANSPLANT MALIGNANCY

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Background: Incidence of malignancy in kidney transplant recipients (KTRs) is known to be higher than that of the general population. Recently, the ageing of the kidney transplant recipient population has lead to an increase in the

number of KTRs who have had pre-transplant malignancies. However, there is no sufficient evidence on whether KTRs treated for pre-transplant malignancies are safe from cancer after KT. In this study, we investigated the development and features of post-transplant malignancies on KTRs with malignancies before kidney transplantation (KT).
Methods: We retrospectively reviewed all patients who underwent KT in our center between March, 1969 and November, 2016. The KTRs divided into two groups with and without pre-transplant malignancy ($n = 71$ and $n = 2664$, respectively). They were compared to patient and donor characteristics, type of malignancy, the incidence of recurrent cancer and de novo cancer, time interval between development of pre-transplant cancer and KT, and post-transplant patient survival were analyzed.
Results: A total number of KTRs with pre-transplant malignancy was 71 patients (2.6%). The most common type of pre-transplant malignancy was thyroid cancer (24.6%), followed by urologic malignancy (21.7%), gastric cancer (11.6%) and hematologic malignancies (11.6%). Three patients (4.2%) were diagnosed with malignancies in the post-transplant period in KTRs with pre-transplant malignancy. Among them, 2 patients presented with recurrent bladder cancer and one case with de novo colon cancer. The incidence of post-transplant malignancy between KTRs with and without pre-transplant malignancy was not a significant difference ($n = 3$, 4.2% and $n = 201$, 7.3%, respectively; $p = 0.29$).
Conclusion: In KTRs who were treated malignancies before KT, the risk of post-transplant malignancy did not increase. Regular surveillance of cancer after KT in KTRs with pre-transplant malignancy is comparably recommended with KTRs without pre-transplant malignancy.

Clinical Lung Cancer

BO045 RISK FACTORS FOR NONMELANOMA SKIN CANCER AFTER LUNG TRANSPLANTATION

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Background: The prevalence of nonmelanoma skin cancer (NMSC) is elevated in organ transplant recipients (OTRs). Known risk factors are fair skin, male sex, age, history of NMSC before transplantation and duration and type of immunosuppressive medication. Prospective, randomized trials have shown a decreased risk for NMSC after switching renal transplant recipients to mTORis. Equivalent data for lung transplant recipients have yet to be determined. As these patients are prescribed higher dosages and triple immunosuppressive therapy, they are at even higher risk for post-transplant NMSC and thus of major interest.
Method: Between 2005 and 2011, a prospective, randomized, open label trial comparing the safety and efficacy of everolimus vs. mycophenolate mofetil each combined with cyclosporine A and prednisolone was performed in 190 lung transplant recipients. In 2015, we recruited from both study arms a total of 90 patients for assessment of individual risk factors for NMSC and dermatologic exam including dermoscopy and optical coherence tomography.
Results: After median follow-up of 101 months, the prevalences for NMSC or its precursors were 37.8%, for precursors 35.6% and for NMSC 17.8%. Risk factors in multivariate analysis were male sex (OR 4.01, 95% CI 1.43 – 11.22, $p = .008$), higher age at first transplantation (OR 1.09, 95% CI 1.01 – 1.12, $p = .02$) and fair skin (OR 3.01, 95% CI 1.02 – 8.93, $p = .047$). Both, immunosuppression with mTORi at date of screening and long-term immunosuppression with mTORi were not associated with decreased prevalence of NMSC or its precursors.
Conclusion: Lung transplant recipients often develop NMSC or its precursors. Male, older patients with fair skin are at greater risk. The investigated immunosuppressive regimens with or without mTORi did not alter the risk for NMSC after transplantation. However, the number of patients is too small to draw definitive conclusion of the relevance of the immunosuppressive regimen in lung transplant recipients.

Clinical Pancreas/Islet Cancer

BO046 PREVALENCE AND SURVIVAL OF CANCER AFTER PANCREAS-KIDNEY TRANSPLANTATION

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Background: Malignancy is an important cause of mortality in solid organ transplantation. However, there have been few studies of de novo malignancy after pancreas-kidney transplantation (PKT). The aim of this study was analyze the prevalence of de novo solid organ malignancy (NSOM) and transplant outcomes.
Methods: We studied the development of NSOM after PKT in our centre from May 1990 to February 2017. We analyzed demographic characteristics, prevalence of cancer and survival of both patient and grafts after cancer diagnosis. We excluded nonmelanoma skin cancer and patients with history of malignancy before transplantation.
Results: We included 194 patients who received 206 PKT (184 simultaneous pancreas kidney (SPK) and 22 pancreas after kidney (PAK)) with triple immunosuppressive therapy and Basiliximab in more than 95%. The mean age at transplantation was 39 ± 7 years and 74% were male. 12 patients developed malignancies (6.1%). Median time from transplant to NSOM was 6.6 (IQR 0.2–11.7) years. The malignancies were: 2 carcinoid tumors, 2 hematologic tumors, 2 breast, 1 melanoma, 1 native kidney, 1 brain tumor, 1 bladder, 1 prostate and leiomyosarcoma. 35 of the 194 patients of the whole cohort died throughout the follow-up, of which 4 recipients died after NSOM diagnosis (11.4%). Patient and grafts survivals were lower in recipients with tumor compared with recipients without tumor (although no statistical significance was found, probably by the low sample size): renal graft survival was 80% versus 90% at 10 years ($p = 0.86$); and pancreatic graft survival was 45% versus 70% at 10 years ($p = 0.15$), respectively. The mean patient survival time from the diagnosis of cancer was 36.6 (IQR 18–54) months. Patient survival after NSOM diagnosis was 90% at 1 year and 50% at 5 years.
Conclusion: The prevalence of NSOM in our PKT recipients is low, in spite of the scarce series of published data for comparison. Also hematological tumors rate is very low, possibly influenced by age and type of induction.

Clinical Kidney Cancer

BO047 DESENSITIZATION PROTOCOL IN LIVING DONOR KIDNEY TRANSPLANTATION DOES NOT INCREASE THE RISK OF CANCER

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Introduction: Incompatibilities is a challenge in kidney transplantation. Potent immunosuppression approach based on desensitization protocols (DS) are needed; However, controversies in publish results, and lack information related to cancer risk is not well documented. Our aim is study the incidence and behaviour of posttransplant malignancies in transplant patients under DS.
Method: Living Donor Kidney transplants (LDKT, 2006–2015) were enrolled. Incompatible patients receiving rituximab, plasma exchange/ immunoadsorption and IGIV were comparing with compatible LDKT. All patients signed inform consent, and the study was approved by the Ethics Committee of our Institution.
Results: 486 LDKT were included, 105 receiving DS before the transplant (ABOi:66, Positive crossmatch:33, Both:4, Others: 2). Median age: 47.94 + / −13.645 (20–82); 61.3% males. Patient/graft survival: 94.4%/86.4%. 77 tumors in 42 patients (8.6%). 51 NMSC (in 16 patients), and 26 non- skin tumors: 21 solid organ tumors (5 lung; 4 prostate, 3 kidney, others), 4 PTLD, and 1 Kaposi sarcoma. 14.4% pretransplant neoplasia. 73.2% of patients with neoplasia were under CNI, 14.6% mTORi, and 9.8% both. sCr at tumor: 1.57 + /- 0.76 mg/dl. Patient survival ($p < 0.05$), age at transplant ($p = 0.031$), and *de novo* CNI ($p = 0.10$) were significantly associated with neoplasia. Cancer causes death (30.8%). CNI *de novo* ($p = 0.039$) and *at-tumor* ($p = 0.043$),

smoking habit (p = 0.01), and neoplasia (p = 0.000) were associated with death. However, DS, induction therapy or mTOR inhibitors were not associated with neoplasia or patient death. More acute rejection (p = 0.001), graft loss (p = 0.025), etiology of CKD (p = 0.009), and induction therapy (p = 0.001) were associated with DS. However, DS was not associated with the appearance of neoplasia, graft loss due to cancer, either death by neoplasia.
Conclusion: The use of DS protocol is not associated with posttransplant malignancy either death by neoplasia in incompatibility LDKT.

BO048 IS LOW/INTERMEDIATE RISK PROSTATE CANCER STILL A CONTRAINDICATION FOR RENAL TRANSPLANT?

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Introduction: Historically active prostate cancer (PCa) has ruled out the possibility of being considered for a renal transplant. PCa is now categorised into low, intermediate and high risk. Treatment options discussed with Low / intermediate PCa patients without ESRD are: active surveillance (AS), brachytherapy, external beam radiotherapy, radical prostatectomy (RP) and hormone therapy.
Objective: Demonstrate our experience of managing patients with ESRD being considered for renal transplant and low / intermediate grade PCa.
Methods: A retrospective database of ESRD patients being considered for renal transplant and concomitant PCa was assessed.
Results: During the last 12 years, 15 ESRD patients have been diagnosed with PCa. One patient was found to have asymptomatic metastatic disease with a presenting PSA of 120 ng/ml. 6 were included in an AS protocol, 8 underwent robotic radical prostatectomy (RRP).

8 patients post-RRP; all have undetectable PSA after mean 46 months f/u; 2 received RTx both 6 years post RRP and both have stable renal function; 2 patients are active on the RTxWL; 3 are awaiting activation between 6–12 m post RRP and 1 is suspended for 3 years.

6 patients on the AS protocol; 2 active on RTxWL on AS. 4 transplanted on AS. One was transplanted after 26 months on AS; he died of Oesophagus carcinoma with 93 months PCa progression-free follow-up. The second patient has stable renal function after 41 months f/u; the 3rd had KTx on AS, the Tx failed; regarding PCa he continues on AS. The 4th patient had PCa progression after 2 year AS; treated with Radiotherapy plus hormones, 5 years later he was transplanted.
Conclusion: Our experience suggests that ESRD patients should be offered as the standard treatment option for low/intermediate risk PCa based on individual PCa disease characteristics and RTx options. AS in appropriate ESRD patients may no longer be a contra-indication to RTx.

Clinical Liver Cancer

BO049 HCC RECURRENCE AFTER LIVER TRANSPLANTATION: RISK FACTORS, CHARACTERISTICS AND OUTCOME

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Hepatocellular carcinoma (HCC) is currently the most common indication of liver transplantation (LT). HCC recurrence is still the main complication affecting short and medium term outcome. The aim of this retrospective study is to analyze, in a recent era, risk factors, features, management and outcome of patients who developed HCC recurrence.

Patients and Methods: From January 2008 till September 2014, 192 patients (mean age: 58.9 ± 7.4 years; 80% of male) underwent LT for HCC with underlying liver cirrhosis. Mean follow-up was 43.4 ± 28.2 months. 21 patients (11%) developed HCC recurrence after a mean time to recurrence of 14.7 ± 12.3 months. 6 out of 21 patients received domino livers. Factors significantly associated with recurrence were: previous hepatectomy (p = 0.0018), outside Milan (p = 0.001) or UCSF criteria (p = 0.006) at transplant, AFP (p = 0.037), blood transfusions (p = 0.017), number of nodules (p = 0.004), size of nodules (p < 0.001) and microvascular invasion at pathology (p = 0.007). Recurrence site was the liver (*n* = 3), lungs (*n* = 4) or disseminated (*n* = 14). Treatments of recurrent patients were: wedge resection (*n* = 1), RFA (*n* = 2) or chemotherapy (Sorafenib, GEMOX, *n* = 17). Four patients were under everolimus plus CNI or MMF and 14 others were converted from CNI to EVL after diagnosis. The 5-year patient and disease free survival of the whole cohort was respectively 73% and 71%. Patient survival after diagnosis of recurrence was 50% at 1 year and 19% at 3 years. Survival was significantly better (p = 0.01) in the group converted to EVL and treated with Sorafenib (*n* = 13) than in the group treated with other strategies (*n* = 6), 67% and 23% *vs.* 50% and 0% respectively at 1 year and 3 years.
Conclusion: In this large cohort, HCC recurrence was relatively low occurring mainly in patients with HCC outside Milan/UCSF criteria. The prognostic of patients after recurrence is dramatic but less rapidly when patients were converted to EVL and treated with Sorafenib.

Clinical Kidney Cancer

BO050 IMAGE-GUIDED THERMAL ABLATION IN DE NOVO RENAL TUMORS ARISING IN KIDNEY ALLOGRAFT: A TWO CASE REPORT

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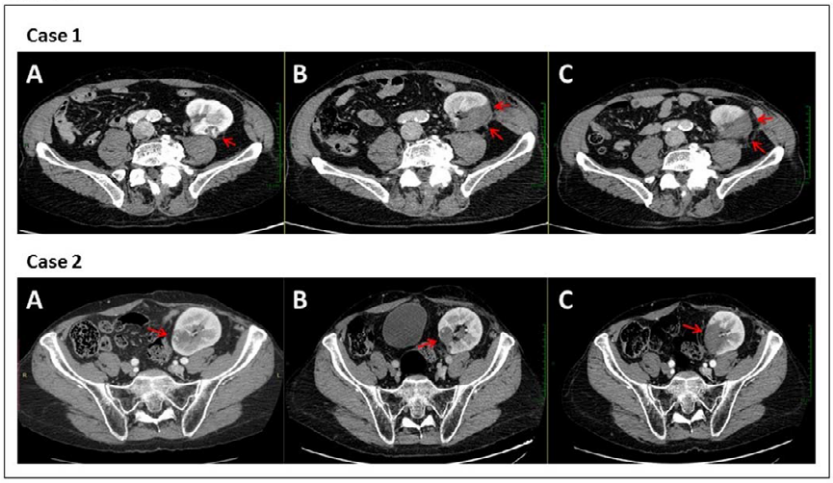
De novo tumors in renal allograft recipients is a severe complication during the long term follow up after transplantation. Tumors located within the renal allograft are not frequent, and once diagnosed are frequently difficult to be treated with conventional surgery and may be end up to transplantectomy. Herein we present two cases of de novo renal tumors arising in the renal allograft treated with the less invasive radiofrequency thermal ablation.

Both tumors were detected during the routine annual follow-up in two patients (aged 68 and 62 years) with excellent renal function (creatinine 1.43 and 1.10 mg/dl) that had received renal transplantation in 1989 and 1994. In both cases, computerized tomography (CT) showed a mass in the pole of the allograft whose shape, vascularization and density suggested the presence of a solid, malignant mass located very close to the calyxes. Maximal diameter of both masses was less than 20 mm.

CT-guided successful thermoablation was performed at the beginning of December 2016 and the immediate outcome was verified by a control-CT, just after the intervention. No residual pathological tissue was evidenced; no major bleeding nor damage to the adjacent parenchyma occurred. Patients were discharged on day 2 and 5, with stable renal function (creatinine 1.53 and 0.99 mg/dl). At 1 month follow-up no significant change of renal function was observed and the contrast-enhanced CT scan did not show any recurrence, neovascularization or damage to the adjacent microcirculation. Figure 1. The 6 month follow-up will be presented.

In conclusion, percutaneous thermal ablation of small renal tumors occurring in renal allografts can be considered a function sparing, safe and effective therapeutic option, when difficult surgical removal may be anticipated. Our experience also supports the absolute need of yearly renal allograft ultrasound follow-up, for early identification of small neoplasm than can be treated less invasively.

Figure 1



Abdominal CT scan of two patients with kidney allograft tumor successfully treated by percutaneous radiofrequency ablation:
A. Kidney allograft tumoral mass at the time of diagnosis
B. Post-procedure result
C. One-month follow-up result

Clinical Liver Cancer

BO051

PREDICTION OF SALVAGE LIVER TRANSPLANTATION FOR HCC RECURRENCE: WHEN AND WHICH PATIENT SHOULD WE DECIDE TRANSPLANT?

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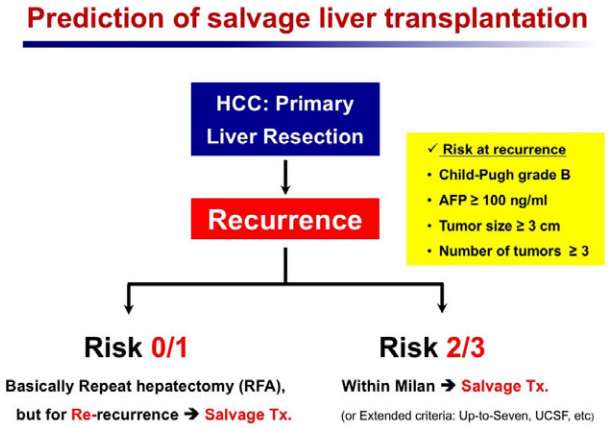
Background: Hepatectomy (Hr) should be the first approach for hepatocellular-carcinoma (HCC) with favorable hepatic reserve. In recurrent HCCs, salvage liver transplantation (LT) is a privileged option to remove recurrent potential with total replacement of liver. However the indication and timing of salvage approach have been debated topics.
Materials and Methods: To clarify patient-selection and timing of salvage LT, HCC-patients with intra-hepatic recurrence after initial Hr (n=212) were retrospectively analyzed and compared with primary LT for HCC (n=60).
Results: Treatment of recurrent-HCCs consisted of Repeat-Hr (n=46), RFA (n=102), and TAE (n=64). The 1/3/5-year post-recurrence overall-survival (OS) were 84/62/28%; 88/57/27%; and 56/10/0%, respectively, in the Repeat-Hr, RFA, and TAE. Multivariate-analysis identified tumor size ≥ 3 cm, tumor number ≥ 3, AFP ≥ 100 ng/ml, and hepatic reserve: Child-B as significant risk factors. A scoring-system using 1-point for each risk factor provided a well-categorized predictive model. The 2-/5-year OS were 92/67%, 83/46%, 52/7%, and 11/0% at risk number (R) R0, R1, R2, and R3, respectively. With regard to LT, the 2-/5-/10-year OS in the within-Milan (n=43) were 87/84/84%, while those in the over-Milan (n=17) were 70/54/45%. Comparing recurrent-HCCs with LT, the R0/1-prognosis was equivalent to that of LT for within-Milan until the 3rd year, however it showed poorer prognosis after the 3rd year due to re-recurrence (2nd recurrence). And 15% of patients with R2/3 met Milan-criteria at the recurrence, who could be good candidates for salvage approach.
Conclusion: In R0/1-HCC recurrence, patients could be tenacious of loco-regional therapy including Repeat-Hr as first approach, whereas 2nd recurrence in R0/1 after the 3rd year or some limited cases in R2/3 should be salvaged by LT.



Basic Kidney Cancer

BO052

LOSS OF REGULATORY ANTI-ANGIOGENIC PROTEASE ACTIVATED RECEPTOR-1 (PAR-1) ANTIBODIES ASSOCIATE WITH THE DEVELOPMENT OF METASTATIC CANCER POST RENAL TRANSPLANTATION AND PATIENT DEATH

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Background: Activated angiogenesis and impaired host immune response contribute to cancers in renal transplant recipients. Induction of VEGF is crucial for neoangiogenesis in tumors. Functional autoantibodies targeting GPCRs are able to induce endothelial dysfunction. We hypothesized that autoimmune GPCR targeting process may disturb VEGF induced angiogenesis. We identified in an in vitro model PAR-1 as a novel activating autoantibody target and assessed the presence of this naturally occurring blocking antibodies in 20 Kidney Transplant Recipients (KTR) with and 29 KTR without metastatic cancer.
Methods/Materials: Human endothelial cells were stimulated with IgG isolated from sera of kidney transplant recipients (KTx-IgG). Transcriptional regulation of VEGF was studied by promoter deletion assay. Transcription factor activation and binding was assessed by qRT-PCR, western blot, EMSA and cFOS knockdown. VEGF secretion was determined by ELISA. Tube formation on Matrigel served to study endothelial neoangiogenic response. All 49 patients enrolled had sera for assessment of PARab via ELISA in 2016 and at the time of transplantation.
Results: Treatment with KTx-IgG reduced ERK1/2 dependent VEGF secretion and tube formation. VEGF secretion and endothelial tube formation could be only normalized by pretreatment with specific PAR-1 inhibitor. KTx-IgG contributed to deregulated neoangiogenesis via reduced VEGF-promoter activity and increased cFos protein expression via its binding to the VEGF promoter. PARab levels were lower at the time of transplant in KTR who developed cancer after transplant compared to those who did not. Levels were also different at the time of cancer diagnosis compared to those who had not developed cancer when assessed in 2016.

Conclusion: We identified the PAR-1 receptor as a new target for functional antibodies in the context of kidney transplantation and tumor angiogenesis. PAR-1 regulated angiogenesis could offer new possibilities.

Basic Others Histology

BO053 GASTROINTESTINAL STROMAL TUMOR DIAGNOSED DURING DONOR PROCUREMENT: DESCRIPTION OF 5 CASES FROM A SINGLE INSTITUTION

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Background: Gastrointestinal stromal tumors (GISTs) are rare neoplasms, accounting for 5% of all sarcomas. Yet, they represent the most common mesenchymal tumors within the gastrointestinal (GI) tract. GISTs occur throughout the GI tract, the stomach being the most frequent site of origin. Herein we describe five cases of GISTs diagnosed during donor procurement.
Methods/Material: Cases were retrieved from the files of the Institute of Histopathology and Molecular Diagnosis, University of Florence, Careggi Hospital, Florence, Italy. Five GISTs were identified out of 847 biopsies analyzed during donor procurement from 2011 to 2016. All candidate subjects were selected as donor by the Tuscany Regional Center Allocation of Organs and Tissues (CRAOT) and National Transplant Center (CNT). No history of cancer was known before the donor procurement. Frozen sections of the tumors were highly suspicious for GISTs, and mitotic count evaluation was also performed. However, the definitive diagnosis and risk assessment required immunohistochemical staining for CD117 and DOG-1 together with the mitotic count performed on permanent sections. The diagnosis of GIST was made according to the morphological and immunohistochemical criteria of Miettinen et al. Mitotic activity was evaluated on 50 consecutive high-power-fields (HPFs). Clinical-pathological studies and follow-up data were provided by the CRAOT.
Results: From our five donors, 2 kidneys and 1 liver were transplanted with no evidence of donor transmitted neoplasia after 18 and 46 months respectively.
Conclusion: We described 5 cases of GISTs with no risk of progressive disease (size <2 cm, mitotic index <5/50 HPFs). In accordance with the latest guidelines of The European Committee on Organ Transplantation, only donors with small gastric GIST are accepted for liver and renal transplant.

Clinical Kidney Cancer

BO054 MALIGNANCIES AFTER KIDNEY TRANSPLANTATIONS AT THE OSAKA UNIVERSITY TRANSPLANT GROUP

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Background: It is considered that the risk of malignancies in kidney transplantation recipients is about 3 to 5 times higher than in general population because of having immunosuppressants. Malignancy is one of the most common causes of patient death with functioning graft. Therefore, it is important how to diagnose and treat malignancies earlier. The aim of this study is to investigate the prevalence of malignancies after renal transplantation and to discuss its examinations and treatments.
Methods: From 1965 to 2016, 1953 patients have received kidney transplantations at the Osaka University Transplant Group hospitals. The incidence of malignancies, clinical courses, and treatment outcomes were analyzed.
Results: The overall incidence of malignancies was 10.2% (200 patients). Of the patients, 178 patients had malignant tumor in single organ, 19 in two organs and 3 in three organs. Death censored graft survival rate and overall survival rate of recipients who have malignancies were 83.5% (no malignancies; 76.2%) and 84.3% (no malignancies; 89.9%) at 10 years, respectively. The cumulative incidence of malignancies was 2.3% at 60 months, 7.2% at 120 months, and 16.9% at 240 months. Post-transplantation lymphoproliferative disorder (PTLD) was the most common malignancy and 35 recipients were diagnosed.
Conclusions: With these data, we speculated that over immunosuppression might induce not only better graft survival rate but also malignancies. We should take care not to be over immunosuppression. On the other hand, we should consider when and how to start to examine for each type of malignancy after kidney transplantation.

Clinical Liver Cancer

BO055 IS THERE ANY DIFFERENCE BETWEEN ABO-INCOMPATIBLE AND ABO-COMPATIBLE LIVER TRANSPLANTATION? ONCOLOGIC ASPECT

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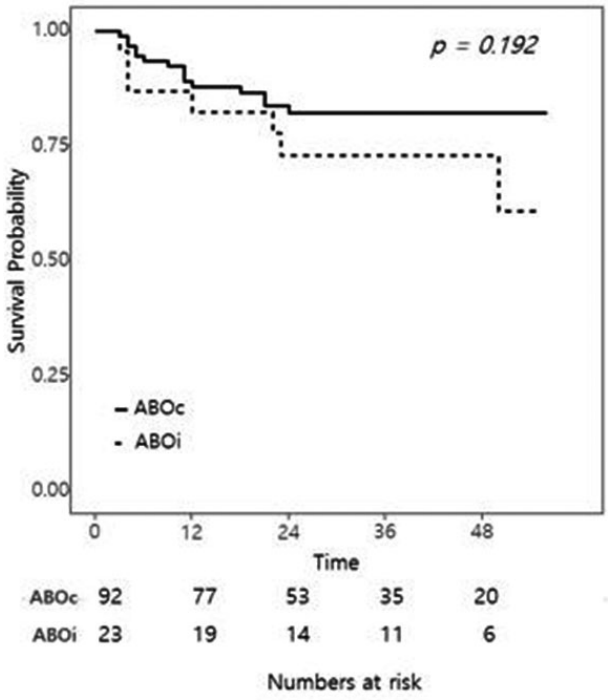
Introduction: Liver transplantation (LT) is increasing treatment option for hepatocellular carcinoma (HCC) in East Asia. Over-immunosuppression is risk factor for oncologic outcome after transplantation and the recurrent HCC is the major cause of graft failure and patient death. But, there are few reports comparing the recurrence of HCC after ABO-incompatible (ABOi) LT and ABO-compatible (ABOc) LT. We analyzed post-transplantation recurrence survival of HCC after ABOi and ABOc liver transplantation.
Methods: A total 115 recipients with HCC who underwent liver transplantation between January 2010 and December 2015 in Severance hospital were retrospectively reviewed. Among 115 patients, 23 patients underwent ABOi LT. We compared the characteristics and recurrence free survival of HCC after ABOi and ABOc liver LT.
The results: There was no significant difference of characteristics between ABOc and ABOi LT. Among 115 patients, 16.3% of patients underwent ABOc LT and 30.4% of patients underwent ABOi LT were recurred. One and 3-year recurrence-free survival rates were 87.9% and 82.1% for the ABOc LT group and 82.4% and 72.9% for the ABOi LT, respectively. When we performed multivariate analysis, high AFP level was the only independent risk factor for HCC recurrence.
Conclusion: The HCC recurrence survival of ABOi LT was comparable to that of ABOc LT. ABO-incompatible liver transplantation is safe and feasible for hepatocellular carcinoma patients.



Variables	ABOc LT (n=92)	ABOi LT (n=23)	p value
Age	54.0 [37–68]	53.0 [48–65]	0.544
Male, n (%)	79 (85.9%)	20 (87.0%)	>0.99
Etiology of liver disease, n (%)			0.963
HBV	79 (85.9%)	21 (91.3%)	
HCV	5 (5.5%)	1 (4.3%)	
Alcoholic	3 (3.3%)	0 (0.0%)	
Others	5 (5.5%)	1 (4.3%)	
Milan criteria			0.863
within Milan criteria	72 (78.3%)	19 (82.6%)	
above Milan criteria	20 (21.7%)	4 (17.4%)	
Preoperative AFP	8.7 [0.88–2410.72]	6.4 [1.84–565.74]	0.388
Preoperative PIVKA II	28.0 [5–29612]	39.0 [14–590]	0.087
UCSF criteria			0.88
within UCSF	64 (69.6%)	15 (65.2%)	
above UCSF	28 (30.4%)	8 (34.8%)	
Number of HCC	2.0 [0–44]	3.0 [0–5]	0.212
Histologic grade			0.582
No residual tumor	11 (12.0%)	1 (4.3%)	
Grade I	5 (5.4%)	2 (8.7%)	
Grade II	41 (44.6%)	8 (34.8%)	
Grade III	30 (32.6%)	9 (39.1%)	
Grade IV	1 (1.1%)	1 (4.3%)	
CCC-Combined	4 (4.3%)	2 (8.7%)	
Microvascular invasion	19 (20.7%)	6 (26.1%)	0.777
Satellite nodule	9 (9.8%)	5 (21.7%)	0.226
Use of mTOR inhibitor, n (%)	25 (27.2%)	10 (43.5%)	0.205

BO056 LIVER TRANSPLANTATION IN A SERIES OF THE 22 PATIENTS WITH UNRESECTABLE BILATERAL NEUROENDOCRINE METASTASES

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Background: Neuroendocrine tumors are rare neoplasms that present bilateral liver metastases at diagnosis. Because of the good initial results obtained, liver transplantation is considered as a potentially curative treatment.

The aim is to present our experience in liver transplantation in a series of 22 patients with unresectable bilateral hepatic metastases of neuroendocrine origin.

Patients and Methods: We retrospectively reviewed the medical records of 22 patients (12 men and 10 women), with a mean age of 49.7 years, who underwent liver transplantation due to bilateral neuroendocrine liver metastases during 20 years. The most frequent location of the primary tumor was the pancreas in 13 patients (2 carcinoid, 3 gastrinoma, 1 glucagonoma and 8 non-functioning tumors). The remaining 9 tumors were located in the small bowel (7) and in the lung (2).

Results: Only 1 patient died due to technical complications related to the transplant, representing a mortality rate for the entire group of 4.5%. After a median follow-up of 10 years (range: 1 month-20 years), two patients died due to tumoral recurrence at 15 and 17 months. The survival rate at 3 and 5 years was 86% and 57%, respectively.

Conclusions: In our series, the results the liver transplantation in the management of unresectable neuroendocrine liver metastases indicate that careful patient selection is required. The key to obtaining good results is individualization of the indication for this procedure.

Basic Others Donation and donor types

BO057 DECEASED ORGAN DONATION AND TRANSPLANTATION ACTIVITY IN THE KINGDOM OF SAUDI ARABIA A 20 YEAR PERSPECTIVE: 1997–2006 VS. 2007–2016

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Saudi Center for Organ Transplantation, Saudi Arabia

Background: Organ transplantation is the best existing method for the treatment of end-stage organ failure. 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 & Materials: A retrospective study comparing the nationwide figures and composition of the Critical Pathway of DD cases for 20 years from 1997 to 2006 compared with 2007–2016 of the Saudi Center for Organ Transplantation (SCOT).

Results: A remarkable increase in the total number of possible DD cases from 3884 of 1997–2006 to 5881 (+51%) of 2007–2016. Mean possible case per year in relation to the number of population for the first half of the 20 year period is 17.7 pmp as compared to 20.7 pmp on the latter. Conversion from possible to potential is 59% (2366 and 3489 respectively). Eligible donors ascend its number from 2030 to 2814 (+38.6%) of which 530 (26% with 2.4 pmp) and 985 (35% with 3.4 pmp) respectively were consented for organ donation. Actual DD for the year 1997–2006 was 538 and 856 (+59%) for the year 2007–2016. There was a significant increase of 99.3% in the number of organs transplanted, from 1160 to 2313 and there was an increase of 31.3% (628 and 825 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 latter period. There was a significant increase in the actual DD. 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.

Basic Others Other

BO058 THE FIRST YEARS OF EXPERIENCE WITH STAND-ALONE ORGAN PROCUREMENT TEAM ERASMUS MC ROTTERDAM

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Erasmus Mc, The Netherlands

Background: In 2009, the Ministry of Health gave instructions to the university hospitals in the Netherlands to implement a master plan to increase the number of organ donors. The Leiden University Hospital started in 2009 and the Erasmus MC started in 2012 with the realization of a stand-alone Multi-Organ Donation (MOD) team to improve quality, reduce the waiting time for the family and relieve the donor hospitals, so that no planned surgery has to be cancelled due to staff utilization.

In this abstract we describe the first experiences and results of the first 3 years of this team.

Method: This team contains: a certified surgeon, an assistant surgeon, an anesthesiologist and two surgical assistants.

The team carries out the MOD completely independent. In a special ambulance they take all the disposables and reusable materials that are needed during the MOD. The team will only use an empty OR room in the donor hospital. The team works in 24 h service connection, and is on call every other week with the Leiden transplant team.

Results: In the first 3 years, no elective surgery had to be cancelled. Compared with the year before implementation, waiting times for the family of the donor reduced with 300 min. Realization of a faster and more efficient procedure by experienced teams led to a reduction in surgery duration of 40 min per procedure. In one year the team retrieved 80 kidneys of which 74 were transplanted. In the same period 30 livers were procured and all used for transplantation. A survey showed very good satisfaction of the donor hospitals with the effort of the MOD team.

Conclusion: In all areas the stand-alone MOD team is showing improvement. No donor hospital surgery had to be cancelled. Waiting time for the family was reduced with 5 h. The procedures are carried out more quickly with good outcome of the procured organs. In conclusion, the implementation of a stand-alone MOD team was a success, and is now structurally implemented in the Netherlands.

Basic Others Donation and donor types

BO059

DEVELOPMENT OF KEY INTERVENTIONS AND QUALITY INDICATORS FOR THE MANAGEMENT OF AN ADULT POTENTIAL DONOR AFTER BRAIN DEATH: A RAND MODIFIED DELPHI APPROACH

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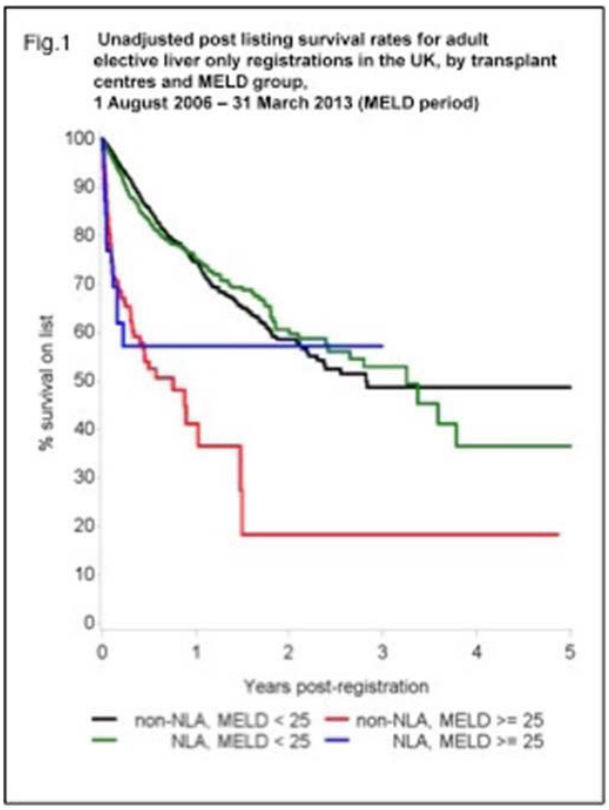
Background: A substantial degree of variability in practices exists amongst donor hospitals regarding the donor detection, determination of brain death, application of donor management techniques or achievement of donor management goals. A possible strategy to standardize the donation process and to optimize outcomes could lie in the implementation of a care pathway. The aim of the study was to identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact.
Methods/Materials: A RAND modified three-round Delphi approach was used to build consensus about potential key interventions and quality indicators identified in existing guidelines, review articles, process flow diagrams and the results of the Organ Donation European Quality System (ODEQUS) project. Comments and additional key interventions and quality indicators, identified in the first round, were evaluated in the following rounds and a subsequent physical meeting. This was conducted over a 4 month time period in 2016.
Results: A multidisciplinary panel consisting of 18 Belgian experts completed the three Delphi rounds. Out of a total of 80 key interventions assessed throughout the Delphi process, 65 were considered to contribute to the quality of care for the management of a potential donor after brain death (DBD); 11 out of 12 quality indicators were validated for relevance and feasibility. Detection of all potential DBD in the intensive care unit and documentation of cause of no donation were rated as the most important quality indicators.
Conclusion: Using a Delphi approach, consensus was reached for a set of 65 key interventions and 11 quality indicators in the management of a potential DBD. This set is considered to be universally applicable in quality improvement programs for the care of potential DBD.



Clinical Liver Allocation

BO060

THE NORTHERN LIVER ALLIANCE (NLA): SUPRA-REGIONAL PRIORITISATION BY SEVERITY

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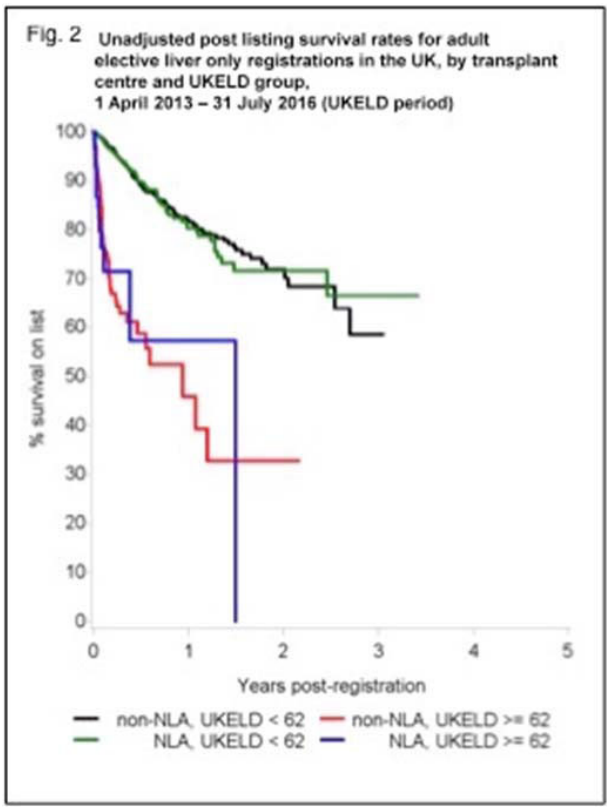
Background: Currently in the UK deceased donor liver grafts for transplantation are allocated to centres rather than a named patient. The Northern Liver Alliance (NLA) Top Band scheme was established in Aug 2006 as a supra-regional allocation system. Donor livers are allocated to patients from 3 UK transplant centres (Edinburgh, Newcastle and Leeds) when their MELD score is ≥25 (Aug 2006 – Apr 2013) or UKELD score is ≥62 (Apr 2013 – present) registered on a common waiting list. Patients are prioritised by severity score. Livers from deceased donors are shared between the centres to improve organ availability for the sickest patients on the elective waiting list. An organ 'payback' scheme ensures no centre is disadvantaged.
Methods: We performed a retrospective review of patients listed on the NLA Top Band from Aug 2006 to Jul 2016. The Kaplan-Meier method was used to predict waiting list survival (WLS) and waiting time (WT) to transplant, comparing NLA Top Band with all patients with MELD≥25/UKELD≥62 from non-NLA centres. A separate analysis compared the pre-NLA period (1996–2006) with the post-NLA period for WT. Comparisons were made using the log-rank test for significance.
Results: 88% NLA top band patients were transplanted over 10 years. The analysis compared 233 NLA patients registered as top band with 523 non-NLA top band patients. WLS was significantly greater for NLA top band patients ($p<0.0001$) for both MELD and UKELD periods (fig. 1 and fig. 2). Median WT to transplant was significantly shorter at NLA centres (15 vs. 58 days). WT was significantly shorter at the three centres in the post-NLA period (15 vs. 122 days).
Conclusions: The NLA improved WLS for patients with MELD≥25/UKELD ≥62 compared to non-NLA centres. WT to transplant improved, likely translating into an improvement in survival. Further analyses to be performed will investigate the effect the NLA has on non-top band patients at NLA centres and whether the NLA affects disease course.



Clinical Others Other

BO061 TEN YEARS OF A VIGILANCE SYSTEM FOR ORGANS, TISSUES AND CELLS IN ANDALUSIA, A SPANISH REGION OF 8.4 MILLION INHABITANTS

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Regional Transplant Organisation of Andalusia, Spain

Background: This work describes a regional V&S system for organs, T&C in Andalusia, a region in southern Spain with a population of 8.42 million inhabitants.
Methods/Materials: We elaborated a practical guidance agreed with the different experts in the field containing a common protocol for the whole region. It also incorporated vigilance tools for evaluation and grading of SAER adapted from the EUSTITE project. We participate actively in SAER investigations as Competent Authority (CA), using experts in the field to assist in investigation and evaluation. We report annually to the national CA, who reports to the EC. Our aim is not only to quantify report activity, but also to foster a culture of report. Along the last ten years we have included the vigilance in training courses and in periodic meetings with our organs, T&C transplant teams in order to reduce fear to report.
Results: We received 369 notifications since 2007 (77% affecting different T&C, 17% organs, 5% both of them and 2.2% relating to the donor). Musculoskeletal (26%) and ocular (27%) tissues, kidney (11%) and liver (7%) are the most frequently implied. The number of notifications has increased progressively from 2007 to the end of 2016 (1, 3, 26, 43, 44, 35, 47, 49, 71, 50 respectively). Reports arrive from a wide range of people in different places and different professional roles, but mainly from tissue establishments.
Conclusions: Having into account that a V&S system is a quality tool, we considered necessary that all the professionals who participate in the whole process from donation to transplantation must know the current protocol in order to detect problems and to take corrective measures as soon as possible, but it is necessary to foster a culture of report among all of them. Increasing of reporting SAER progressively along the last ten years reveals an increase of awareness among users in our region which is probably contributing to improve the quality and safety of organs, T&C.

Clinical Others Donation and donor types

BO062 BRAIN DEATH AND DONOR MANAGEMENT DURING 13 YEARS IN AKDENIZ UNIVERSITY

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[1]Anesthesiology and ICU Department, Akdeniz University Hospital, Turkey; [2]Akdeniz University Hospital, Organ Transplantation Center, Turkey

Introduction: The diagnosis and incidence of brain death and donor management were investigated in Akdeniz University ICU.
Materials and Methods: Records of 411 brain death patients admitted to ICU between 2003 and 2016 were evaluated. However, 211 patient's records were found eligible to be included in the study.
Results: Mean age was 37, 68 (2–80) and 141 (58%) of the patients were male. Primary pathology leading to brain death was intracranial hemorrhage in 116 (77.9%) patients. Other causes were tumors (7%), infarcts (3.7%), meningoencephalitis (3.2%) and others. Clinical examinations of 42 (19.7%) patients were compatible with brain death at the time of ICU admission. Mean GCS at emergency room and ICU admission were 7 and 5, respectively. Apnea testing could not be performed in 14 (6.5) patients because of hemodynamic instability or hypoxemia. Brain death diagnosis was confirmed with SPECT (32.8%), Transcranial Doppler USG (26.5%), electroencephalography (24.6%). More than one confirmatory test was used in 26% of patients. Spinal reflexes were observed in 27 (12.6%) patients and two patients had Lazarus sign. Sympathic storm and diabetes insipidus were determined in 33.3% and 57.2% patients. Vasoactive drug infusion was used in 147 (33.8%) patients for improving hemodynamic variables. Organ donation was performed in 139 (33.8%) brain dead patients among 411 patients diagnosed as brain death in 13 years.
Discussion: Brain dead patients are potential organ donors and should be identified and treated immediately. Unsuccessful apnea testing incidence and reasons for brain death was in accordance with other studies. Sympathic storm was less frequent than other studies (33% vs. 63%). Different cultures and nations have various perspectives and regulations in terms of brain death and organ donation which may hamper rapid diagnosis of the potential donors. However, ICU clinicians should be sophisticated and careful about determining brain death and providing donor care.

Clinical Liver Donation and donor types

BO063 SPLIT LIVER TRANSPLANTATION CAN REDUCE MORTALITY ON WAITING LIST: 4 YEARS OF THE CZECH NATIONAL SPLIT LIVER PROGRAM

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Background: Split liver transplantation (SLT) has got potential to help with organ shortage. Until 2013, the pediatric and small adult recipients used to wait the Czech Republic for full size liver graft, only few received partial graft. Morbidity and mortality on the waiting list used to be relatively high. The systematic SLT program has been introduced in Jan 2013, each donor within criteria must be assessed for liver splitting. SLT are used for all types of transplants including fulminant failure and urgent re-transplantation.
Methods: The data were collected prospectively; results of 357 whole liver and 88 SLT performed between 1/2013 and 12/2016 were compared. For waiting list mortality period 1/2006–12/2012 (642 patients listed) and 1/2013–12/2016 (553 patients listed for liver transplantation) were compared.
Results: We performed 45 SLT, of those 29 classical for child and adult, 16 full left/full right for 2 adults/children. SLT received 88 patients, 2 grafts were not used for long cold ischemia. As expected, there was significantly higher biliary complication rate: 14.29 vs. 40.91% ($p < 0.001$), there were 14 (15.91%) resection margin leaks, 20 (22.73%) anastomotic leaks and 7 (7.95%) anastomotic strictures, 18 (50%) required re-operation, only 4 (11.11%) patients required re-transplantation. There was no significant difference in early mortality: 3.08% vs. 6.82% ($p = 0.824$). The mortality on waiting list decreased non-significantly: 8.7 vs. 4% ($p = 0.18$), although there was no death of child on the waiting list since 1/2013 and also no death of an adult in 2015.
Conclusions: SLT program is used since 2013 at our institution for all patients including pediatric, adult, fulminant, re-transplants; some of the urgent cases were ABOi. The rate of biliary complications is high; majority of complications can be treated successfully without need for re-transplant. Despite all the related difficulties SLT program has helped to decrease waiting list mortality.

Clinical Others Donation and donor types

BO064 SPANISH MEDICAL STUDENTS AND DECEASED ORGAN DONATION

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Background: Consistently throughout the last years Spain has a leading position as far as the organ donation rates are concerned. Due to its success it is described as the 'Spanish model', and many countries have tried to adopt it. In this research project we present attitudes, views, and communication patterns about Deceased Organ Donation (DOD).
Methods/Materials: A validated questionnaire was distributed to 159 medical y students of a major Spanish university to explore their attitudes, views, and communication about DOD. The survey was followed by a focus group discussion, following the thematic analysis.
Results: Spanish medical students view DOD as an act of helping others (87%), the believe that scientific facts and figures (67%) are an important reason for supporting DOD, as well as a way for raising awareness and setting an example for other people (62%). The most preferred source of information is medical TV shows and films (53%) and awareness campaigns (52%). The students further analysed the role of awareness campaigns in motivating people and suggested possible ways that medical students could participate in campaigns in Spain and throughout Europe.
Conclusion: Exploring the ways medical students learn, view, and communicate regarding the issue of DOD could inform future educational approaches.

Clinical Liver Donation and donor types

BO065 THE SURGICAL APPROACH TOWARDS DCD LIVER PROCUREMENT: RESULTS OF AN ONLINE SURVEY

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Introduction: Donation after circulatory death (DCD) is a valuable source of liver grafts for transplantation, however there are different approaches among transplant surgeons regarding the donation procedure. Aim of our study is to determine the differences in the approach in procurement of DCD livers among transplant centers in Belgium, Spain, The United Kingdom and The Netherlands.
Methods: An online survey was sent by Survey Monkey® to all surgeons involved in liver transplantation in above-mentioned countries.
Results: The survey had a response rate of 65% (64 out of 98); Of the respondents, 34% limits the age of the DCD donor to 60 years, whereas 64% accepts livers from older donors. We found that the calculation of the first Warm Ischemia Time (WIT) varies substantially between countries: respondents from the UK and Spain start counting WIT at deterioration of saturation/blood pressure (87% and 86%, respectively), whereas in the Netherlands 60% of the respondents use cardiac arrest as starting point of WIT. A majority (80%) states that the trend of transaminases is more important than the last value when deciding to transplant a DCD liver. Eighty-one percent of the respondents perform a super-rapid sternolaparotomy as a procurement technique. Dutch and Belgian surgeons use mainly aortic perfusion (95% and 71%) with UW (95%) and IGL-1 (65%), respectively. Dual perfusion is more common in the UK (87%) and in Spain (86%), in 67% with UW (UK) and in 71% with Celsior (Spain). Liver biopsy before implantation is performed by 73% of the respondents, mostly to determine the percentage of steatosis. Fifty-one percent of the surgeons accept a maximum first warm ischemia time (WIT) of 30 min.
Conclusion: The results of this survey showed important differences in the surgical approach to the DCD liver donation mainly in the perfusion technique and the calculation of the first WIT. The impact of this finding is currently under investigation.

Clinical Others Donation and donor types

BO066 HOW THE RATE OF ORGAN DONATION INCREASED AGAIN IN IRAN

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Introduction: With 2 weeks educating the Organ Procurement Units (OPU) directors and staff we could increase the rate of organ donation in Iran but we realized that they are not able to function ideally without help in their provinces. So we made a group of experts in organ donation process and by sending this group to different provinces helped the OPUs to put their train on the rail.
Material and Methods: A group of experts in different aspects of organ donation (Detection, Brain dead diagnosis and confirmation, Donor Maintenance, Family interview, organ preservation and procurement paperwork) was made. The program named Iranian OPU supporting system (IrOSS). Provinces with higher population but lower PMP were chosen first. The group would go to that province and start motivating and educating (Theoretically and practically) the following groups for one week about organ donation and then for 2 years by periodic travels and strict control of their activities:

1. Authorities including the University director and his/her assistants, Mayor, TV director and religious leaders
2. Director of OPU and the coordinators
3. Brain dead confirmation team
4. Forensics
5. Anesthesiologists and ICU specialists
6. ICU nurses
7. Medical Students
8. Volunteers

Results: IrOSS course has been hold in 5 provinces which its results are presented in table 1.
Conclusion: IrOSS could improve organ donation significantly. It shows that an expert team in every country should get the responsibility of periodic educating and promoting the OPUs to help them for improving their organ donation system.

NO.	OPU	AD/2015 (before IrOSS)	PMP/2015 (before IrOSS)	AD (after IrOSS)/ month	PMP (after IrOSS)
1	Guilan	18	7.2	27/7 month	18
2	Mazandaran	19	7.3	14/5 month	13
3	Bushehr	3	2.9	6/4 month	18
4	East Azarbaijan	8	2	4/3 month	5.2
5	Hamedan	15	8.5	10/5 month	13.7

Translational Others Other

BO067 IMPACT STUDY OF THE EUROPEAN-MEDITERRANEAN POSTGRADUATE PROGRAM ON ORGAN DONATION AND TRANSPLANTATION PROJECT (EMPODAT)

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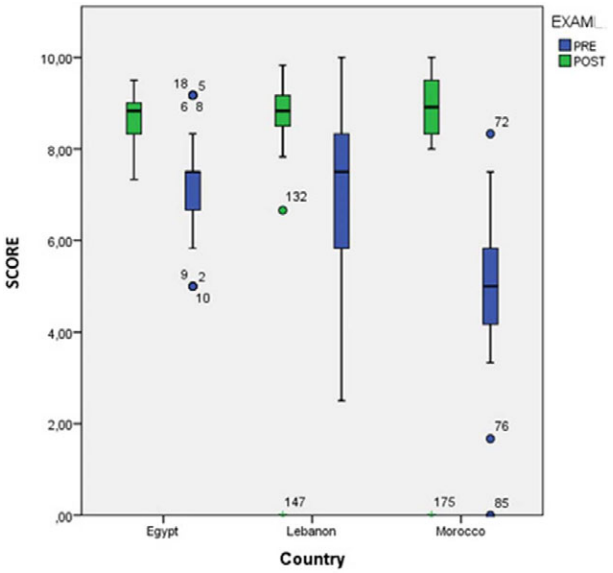
Background: EMPODaT was a TEMPUS product (an Education, Audio-visual and Culture Executive Agency (EACEA) program) to cooperate in higher education programs of Organ Donation & Transplantation in Egypt, Lebanon and Morocco in accordance with the European Space for Higher Education guidelines. The EMPODaT consortium was constituted by 4 European Univ., 1 European Foundation and 6 beneficiary Univ. from Egypt, Lebanon and Morocco.
Methods/Materials: Three evaluations were performed: Donation & Transplantation Diagnosis (DTD), Training and Quality. DTD was carried out before designing the postgraduate curricula and conducted in 3 parts, following different adapted questionnaire methodologies. Training (available in English and French) was designed in 1 academic year of 30 ECTS credits (750–900 h) employing blended learning methodology. Pre- and Post-training tests, self-assessing activities, and traineeship activity charts were used to evaluate the students. For Quality evaluation, assessment questionnaires and semi-structured interviews were conducted.
Results: Beneficiary Univ. reported in DTD Part I a general lack of specific training. Part II was answered by 444 health care students, 62% reported low knowledge on Donation and 72% on Transplantation, being donor management and surgical procedures the less known (77%; 82%). Part III detailed the current transplant/donation activity data in the 3 countries. 90 students were trained 15 per Univ.), 39W–51M, 79 doctors (23% ICU & 22% surgeons) and 11



nurses. Significant differences were found among improvement knowledge between countries.

The main score in the project quality evaluation was 4.2 (scale 1–5).

Conclusion: Specific training was needed in all countries. All did living donation thus the knowledge improvement in organ donation was greater than in transplantation. Morocco was the most beneficiated country obtaining better final scores albeit from lower basis. The project was highly appraised by students.

Translational Others Donation and donor types

BO068 MONITORING DONATION AND TRANSPLANTATION ACTIVITY: THE DONOR ACTION PROGRAM

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Introduction: The Emilia-Romagna region (ERR), a northern Italy region of 4 450 508 inhabitants, in order to achieve quality levels in organ donation, has supported the "Donor Action" program (DA) since 1998, so as to check whether all brain deaths are identified, referred and assessed.

Methods: The program started in July 1998 in 28 ERR Intensive Care Units (ICUs, 254 beds in all), 7 of them belonging to hospitals with neurosurgical department (81 beds in all).

The DA program analyzes the potential donor identification through deceased patient charts in the ERR. The program is utilized by transplant hospital Coordinators through the regional computer network, whose data are collected and analyzed by the CRT-ER.

Results: ICUs total deaths have increased from 1998 to 2016, in the meantime a reduction in the percentage of deaths with severe brain damages on total deaths (43.9% vs. 22.6%) and a remarkable growth of brain death assessments (86 vs. 229) have been seen. Stability of refusals has persisted (Table 1).

Over the years, organ donation has seen a substantial growth (33.3 per million population in 2016), while transplant activity has reached high level quality standards, reporting a remarkable amount of organ transplantations (362 in all in 2016).

Conclusion: These data prove a positive potential donor identification activity in the regional ICUs and transplantation activity in the regional transplant centres thereafter; refusals amount keep on representing an important issue.

DA program confirms to be an efficient quality control program and has helped the ERR system to improve potential donor identification in the ICUs.

	1998 2nd sem	2011	2012	2013	2014	2015	2016
ICUs Total Deaths	649	1774	1764	1638	1636	1832	1767
Severe Brain Damage (SBD)	285	344	414	363	371	429	399
SBD/Total Deaths %	43.9	20.2	23.5	22.2	22.7	23.4	22.6
Brain Death Assessments	86	208	198	188	186	228	229
Organ Donors	55	96	114	111	101	124	143
Refusals (N°/%)	26/33	59/ 34	50/ 26	43/ 23	56/ 33	63/ 30	61/ 27

Clinical Ethics/law/psychosocial/public policy Donation and donor types

BO069 CURRENT STATUS OF FOREIGNERS AND OVERSEAS ORGAN TRANSPLANTS IN KOREA

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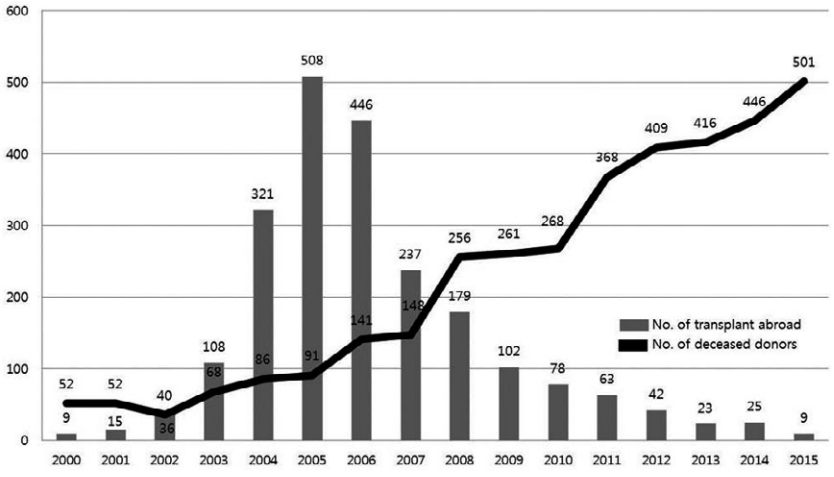
Background: Transplant tourism (TT) have become as an important legal and ethical issue to be discussed at the international society. In this paper, to estimate the prevalence of transplantation tourism, we collected official data available, and conducted a survey on foreigners as well as overseas transplant cases in Korea.

Methods: Data on kidney and liver transplantation (KT & LT) performed abroad were obtained from 42 transplant centers by surveying through transplant coordinators. Data on foreigners transplanted in Korea and deceased organ donors were obtained from KONOS and Korea Organ Donation Agency.

Results: A total of 336 foreigners received organ transplantation (OT) (KT: 174 cases, LT: 162) in Korea from 2006 and 2016. Among foreigner KTs, Mongolian was the most common (32%), followed by Chinese (18%), USA (9%) and Arab Emirate citizens (7%). Among LTs, 39% of cases were from Mongolia. Arab Emirate (23%), China (13%) and USA (6%) were next common countries of origin. A total of 2205 patients were received overseas OT (KT: 976 cases, LT: 1229) between 2000 and 2015. Destination countries for overseas OT revealed that 2149 of the 2205 cases (97.5%) of OT were conducted in China. The number of deceased donors showed negative correlation to the number of overseas transplants. The number of overseas transplants, which was only nine in 2000, drastically increased to 40 cases in 2002 and 508 cases in 2005 (Figure 1). After the announcement of the moratorium on the commercialization of executed criminals' organs in China, the number of overseas transplants in Korea decreased. Especially, the number of transplant tourism cases drastically decreased after 2009 was noted (Figure 1).

Conclusion: National effort to achieve self-sufficiency by increasing activity for organ donations is one of the fundamental solutions to TT. And, cooperation between organ-receiving and organ-supplying countries (revision of the transplantation law in Chi)



BO070 THE GREEK FINANCIAL CRISIS: IMPACT ON ORGAN DONATION AND TRANSPLANTATION

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Background: Greece's debt crisis has had widespread societal impact with its healthcare system taking an especially hard blow. With its healthcare system in freefall, the aim of this study is to assess its effect on organ donation and transplantation in Greece.
Methods/Materials: We analyzed retrospectively data (2001–2016) provided by the Hellenic Transplant Organization, The International Registry in Organ Donation and Transplantation (IRODaT), Eurotransplant, Scandiatransplant, National Health Service Blood (NHSBT) and the Transplant and United Network of Organ Sharing (UNOS) databases.
Results: Organ donation in Greece has been decreasing, averaging 4.6 donors per million people (dpmp) for the last 4 years, with an average of 2.5 organs transplanted per deceased donor, fig. A&B. Despite high transport-related deaths (9.5/105 inhabitants compared to an EU average of 5.9) brain-dead donation remains low. Conversion-to-donation rates were 39% in 2015, fig. D. In 2015, organ donation rates were inferior to Eurotransplant, Scandiatransplant, NHSBT, UNOS and Italy (15.1, 18.8, 20.2, 28.5 and 22.5 dpmp respectively), fig. E. Kidney transplantation (KT) overall and deceased donor KT (DDKT) specifically have been declining. Live donor kidney transplants (LDKT) make up 33.8% of total KT, fig. C. Liver transplantation (LT) is also declining, with a single active transplant center remaining, performing an average of 25.3 LTs annually. Pediatric and living-liver donor transplantation, multi-visceral, small bowel, and whole organ and islet pancreatic transplantation are non-existent.
Conclusion: There has been a sharp downturn in Greek organ donation and transplantation. This has resulted in an efflux of Greeks seeking transplantation abroad with more than 50 million euros public health funds channeled out of the country (2010–2014). Individuals with inadequate independent financial resources to seek transplantation abroad are especially underserved.s

Basic Ethics/law/psychosocial/public policy Other

BO071 GLOBAL QUALITY OF LIFE TRANSPLANT RECIPIENT SURVEY WORLD TRANSPLANT GAMES FEDERATION

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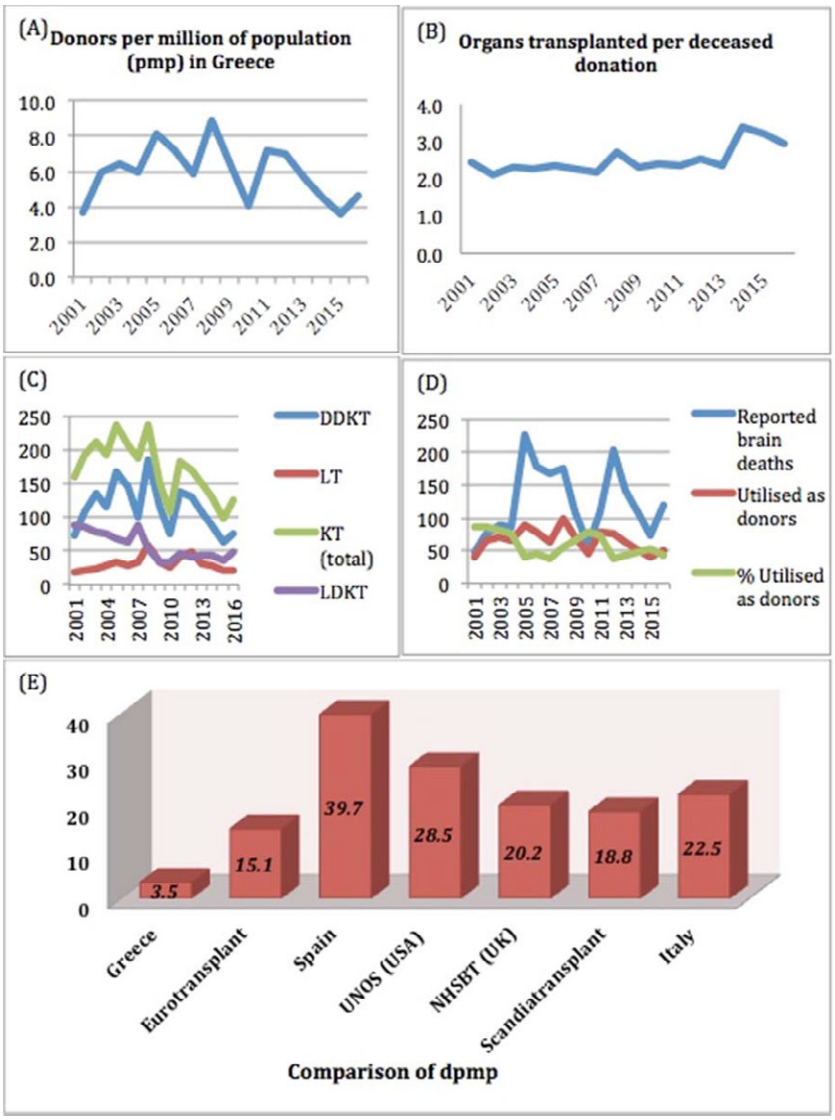
World Transplant Games Federation, United Kingdom

Background: The importance of exercise in all populations is recognised by health authorities across the world. It is generally accepted that this is no different for organ transplant recipients although there is less empirical evidence.

The World Transplant Games Federation has recognised the need to provide pathways from a sedentary life immediately post transplant to activity and movement underpinning a recipient's daily and weekly regime.
Methods: To establish a benchmark, a survey was distributed to 65 member countries. It was released in English and a limited number of other languages. Topics included standard of living, employment, emotional well-being, body composition, exercise and activity and lifestyle factors.
Results: 1216 respondents from 58 countries completed the 39 questions. The benefits of transplantation were clearly evident. 70% of respondents indicated their standard of living had improved significantly since their



transplant. 8% self-reported as being significantly overweight and 32% a little overweight. 25% of respondents were 'extremely keen' and another 25% 'moderately interested' to reduce their weight to improve their health. 'Keeping fit' ranked as the leading reason why recipients participated in sport followed by its 'social aspects' and 'for the competition'. A quarter reported that their transplant medical team recommended that they undertake exercise or sport as part of their rehabilitation only when they were first transplanted. 20% were reminded regularly, 26% occasionally and 28% had never been recommended they undertake exercise or sport. 80% were 'interested' or 'extremely interested' in participating in more sport.
Conclusion: Transplant recipients responding to a survey by the WTGF are motivated to improve their health and well-being and recognised the role of exercise and sport. Despite a high degree of interest to participating in more sport, advice given to them by transplant care providers appears variable and often non-existent.

BO072 ATTITUDES, PERCEPTIONS AND KNOWLEDGE OF EUROPEAN MEDICAL STUDENTS TOWARDS ORGAN AND TISSUE DONATION AND TRANSPLANTATION

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Background: Organ donation and transplantation has become the only option for some final-stage diseases. An adequate training in medical faculties is crucial to assure our future doctors are prepared to face this new reality.
Methods/Materials: An on-line survey about organ and tissue donation and transplantation was distributed through social networks during 2016 to medical students from European universities.
Results: A total of 979 medical students from 147 universities of 30 European countries (female 67.9%, mean age 22.7 years old) responded to the survey. Italy (21.6%), Belgium (10.6%) and Spain (9.4%) were the most responders.

Most of the students would consent to donation of their own organs (88%) or those from their relatives (79.1%) having Austria and Belgium the highest consent rates and Ukraine and Sweden the lowest. The main reason for opposing donation was the lack of knowledge of their relative wishes (28.8%).

A 37.4% of the students were not sure or had misconceptions about the current organ donation legislation in their country. In Sweden, Turkey or Ukraine none of the responders knew about the current legislation.

Most students (65.9%) agreed that death can be diagnosed according to neurological or cardio-circulatory criteria, having Ukraine the highest ratio of agreement and Denmark the lowest, and 73.8% conceptualized correctly brain death as equivalent to death, having Austria the highest ratio and The Netherlands the lowest.

An overall positive attitude towards donation was observed in 96.4% of the students who described the process using positive adjectives, being positive (68.3%) and altruism (67.7%) the most frequently used. Complicated (29.7%) and stressful (11.6%) were the preferred negative terms used to describe it.
Conclusions: European medical students show a positive attitude towards donation and transplantation, although major shortfalls have been identified. Donation and transplantation issues should be included on the university educational curricula.

Clinical Ethics/law/psychosocial/public policy Donation and donor types

BO073 ATTITUDES AMONGST MEDICAL STUDENTS TOWARDS DEATH CONCEPTS AND PROCEDURES RELATED TO ORGAN DONATION

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Background: The EU announced the problem of increasing organ scarcity and estimated that 16 people die daily while waiting for a transplant. Especially Germany is known for low rates for organ donation; opt in is in practice and there is no acceptance for donation after cardiac death. Interestingly, one of the obstacles remains the fear of German politicians and decision makers to discuss openly this topic. We therefore addressed these concerns to evaluate attitudes towards organ donation.
Methods/Materials: As a spin-off project of ESOT-ELPAT we developed a survey which was introduced into the curriculum of medical students at the University of Münster in Germany. Since June 2016 medical students in their 3rd clinical semester were asked to participate with the aim to evaluate beliefs and opinions in regard to death and organ donation. The survey was accompanied by a tutor in case of questions. Multiple answers were possible.
Results: So far 233 medical students were interviewed. Most respondents felt being moderate informed on legal, medical, and psychosocial aspects in death criteria and organ donation. Attitudes towards defining death revealed that mostly "body as whole is non-functional" (86/227) and "person is gone despite some left body functions" (137/227) were accepted. A cranioplasty after craniotomy using bandaging was accepted in 49/229, while 111/229 accepted organ donation once prognosis is fatal without further diagnostics/procedures. Organ donation after cardiac death was accepted in 197/227 responders. The wish of the patient to donate was more appreciated than the legal regulations. Furthermore, organ quality in the process of donation was relevant in decision making for most students.
Conclusion: Attitudes amongst medical students towards death concepts and procedures related to organ donation seem to be liberal, which is in contrast to the taboo of German decision makers. Patient centered decisions were more accepted than legal regulations.

Basic Ethics/law/psychosocial/public policy Donation and donor types

BO074 ROLE OF RELIGION ON RAPID DECEASED ORGAN DONATION RATE IN IRAN

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Background: Transplantation is the treatment of choice for organ failure, but a worldwide shortage of suitable organs exists. We conducted a systematic review of factors affecting improvement deceased solid organ donation rates in Iran.
Methods: An analysis of the last decade, 2006–2016, demonstrated a rapid growth curve for Iran deceased donor organ donation, which increased from 1.8 to 16.3 donors per million population (pmp). We found multiple factors in Iranian population for rapid growth of deceased organ donation including: religious beliefs, cultural background, high education, the altruistic motive of saving lives and improving lives for others, mass media and many others.
Results: The population of Iran is more than 80 million. More than 85% of Iranians are literate. Between 98 and 99 percent are Muslim. Around 80 percent of total Muslims are Shi'a, the rest being Sunni. Christian, Zoroastrian, Jewish communities and other minorities have constituted between 1 and 2 percent of the population. More than 700 liver transplants were done in Iran annually.

Shiraz (center of Fars province in south of Iran) transplant center is the busiest in the world as more than 500 liver transplants were done in last year. More than 95% are from deceased donors. Deceased donor pmp in Fars province in 2016 was 23.8. Almost all of deceased donors are Muslim and belongs to Shi'a branch of Islam.
Conclusion: This review highlights the positive role of Islam on deceased organ donation. The religion of Islam strongly believes in the principle of saving human lives. Almost all of supreme leaders of Islam have permitted the organ transplant from deceased donors as a necessity.

Clinical Ethics/law/psychosocial/public policy Other

BO076 CAN THE BEST PRACTICE INDEX ADMISSION FOR KIDNEY TRANSPLANTATION BE COVERED BY A STANDARD NATIONAL TARIFF? AN ECONOMIC ANALYSIS OF A REPRESENTATIVE COHORT

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Introduction: The National Health Service is undergoing stringent fiscal scrutiny of its services. National tariffs are being constructed to provide lean and efficient services akin to private health models. However currently services are costed using a 'top-down' approach, relying on assumptions and estimations from large hospital databases. Consequently regional tariffs differ vastly for kidney transplantation. There is little in-depth work on patient-level costing (PLC) in this area. We aim to provide a comprehensive 'bottom-up' cost of an uncomplicated adult renal transplant at our centre.

Methods: Retrospective pathway analysis of 48 patients from April 2015 to April 2016 was performed. Data was systematically collected for each index inpatient transplant episode, with deconstruction it into its independent components for costing. Costings were sourced directly from departments. Repeat surgery for complications and critical-care admissions were excluded.
Results: The mean overall cost for a standard adult renal transplant was £15 612 (range £12 048–£33 038). It worked out to £15 983 for deceased donor transplants and £14 868 for living donor transplants. Mean length of stay was 10.3 days (range 6–32). 35.4% required haemodialysis for delayed graft function. 18.8% required additional biopsy. In this cohort no direct correlation was found between graft/recipient factors and cost.
Discussion: The large variation in cost between even 'uncomplicated' transplant patients highlights the individuality of each case. Current costing mechanisms fail to capture the nuances of an inpatient episode; critically missing high cost areas- staff interactions, out-of-hours premiums, biopsies, and haemodialysis. To deliver a best practice national kidney service, it is paramount that baseline costings are accurate. PLC exercises should be utilised to ensure this. It is vital that these costing exercises should model all the numerous variables to ensure centres are correctly reimbursed.

Clinical Ethics/law/psychosocial/public policy Donation and donor types

BO077 COMPLICATED GRIEF AND ORGAN DONATION: ASSESSMENT OF DONORS' RELATIVES AFTER SIX MONTH

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Objective: In 2016, 1774 organ donations were performed in France. Currently, there doesn't exist any sector to orientate donors' families. The purpose of our study is to investigate the complicated grief donors' relatives, its associated diseases and risk factors.
Method: Prospective, single-center, observational study. During the first meeting with the transplantation coordination team of the University Hospital of Bordeaux, France, it was proposed to the organ donors' relatives to participate. The relatives who had accepted received the ICG, IDS-SR and PCLS questionnaires at 1, 3 and 6 months after the death. The primary endpoint was the presence of complicated grief, defined by an ICG>25, among the relatives of organ donors after 6 months from the death. The secondary end points were the presence of major depressive disorders (IDS-SR≥15) and post-traumatic stress disorders (PTSD) (PCLS≥44) at 6 months and the analysis of complicated grief's risk factors.
Results: From December 2014 to January 2016, 81 donors' relatives were included. An average of 3.24 relatives per donor was included. 16 of the 29 relatives who responded at 6 months had an ICG>25. The prevalence of complicated grief is 55.2% [CI 95 = 37–73]. The prevalence of major depressive disorder and PTSD are respectively 72% [CI 95 = 55.7–88.3] and 31% [CI 95 = 14.2–47.8]. No risk factors of complicated grief after 6 months from the death were found in this population.
Conclusion: This study shows a high risk of complicated grief among donor's relatives. The establishment of dedicated channels to orientate these bereaved persons seems important. Further studies should be conducted to define better the complicated grief's risk factors following the organ donation.
Keywords: complicated grief, major depression, post-traumatic stress disorder, organ donation, intensive care

BO078 TRANSPLANTATION OF ORGANS FROM DONORS WITH HEPATITIS C: THE POTENTIAL TO SUBSTANTIALLY INCREASE TRANSPLANT ACTIVITY

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Introduction: Organs from hepatitis C virus positive (HCV+ve) donors are commonly declined for transplantation because of the risk of disease transmission, but new direct acting antivirals (DAA) open up the possibility that organs from such donors could be safely used. A registry analysis was undertaken to determine the potential impact that use of all organs from HCV+ve donors would have on transplant activity and outcome.
Methods: The UK Transplant Registry and the Potential Donor Audit were interrogated to identify anti-HCV antibody positive deceased organ donors over the 16-year period from 01/01/2000 to 31/12/2015. Discarded HCV+ve organ quality was assessed using donor quality indices and functional parameters.
Results: 244 HCV+ve deceased donors were identified, of which only 65 (27%) provided organs used for transplantation in 93 recipients (63 liver and 30 other organ transplants). Unadjusted liver recipient patient and graft survival was not adversely impacted by the donor HCV+ve status. Organs from 146 HCV+ve consented donors were declined for transplantation and in most cases (71.4%) this was because of positive virology rather than poor organ function (8.9%). The median eGFR of declined HCV+ve donors was 103 ml/min/m^2 (IQR 70–144) and 49% had a UK kidney donor risk index score of <1.02, suggesting at least 77% of potential transplanted kidneys from such donors would be functioning at 5 years. 120 eligible donors were not consented for transplantation in the UK because of the presence of HCV. Cost analysis demonstrated that transplanting an HCV+ve kidney into an HCV-ve recipient and treating them with DAA would be cost neutral with dialysis by 4 years after transplantation.
Conclusion: Consideration should be to the use of organs from HCV+ve donors for HCV-ve recipients. Donor kidney quality is generally good and the use appears to be cost effective compared to dialysis when taking into account the need for antiviral therapy after transplantation.

Basic Ethics/law/psychosocial/public policy Other

BO079 EDUCATIONAL INTERVENTIONS EXPANDING THE LIVING KIDNEY DONOR POOL

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Background: Previous research has shown that our home-based educational program for patients with end-stage renal disease (ESRD) may lead up to four times more living donor kidney transplantations (LDKT) than without an educational program. We have investigated the relation between educators' treatment adherence and the effectiveness of the educational program.
Methods/Materials: The health educators held tailored, group educational meetings in the homes of 63 patients. A Treatment Adherence Measure (TAM: Scale 1–5) questionnaire was completed by patients after receiving the education in the presence of the educator (TAM-1). A second TAM (TAM-2) was administrated afterwards by an independent person by telephone. Pre- and post-educational knowledge and communication regarding renal replacement therapies (RRT) were measured using standardized questionnaires. The rate of LKDT was recorded.
Results: TAM-1 scores shows a significant positive relation with both communication attitude (B = 0.832; p = 0.041) and communication frequency (B = 1.368; p = 0.027). The TAM-2 scores showed a significant positive relation knowledge regarding RRT (B = 6.94, CI 95% [1.67–12.22], p = 0.029). No relation was found between any TAM-score and LDKT activities.
Conclusion/Discussion: Given that there is an indication that program effectivity is related to educators' treatment adherence, it is relevant to monitor the quality of the program. Currently, our home-based educational program is implemented in four regions in The Netherlands. The first objective of this implementation is to map the generalizability of previous research, while maintaining quality, by creating a quality assurance framework. Second, to convince policymakers that this home-based education needs to become standard care, a cost-effectiveness assessment is warranted for the program, as well as for the quality control system.

Clinical Ethics/law/psychosocial/public policy Immunosuppressive agents

BO080 INTEGRATING MENTAL AND PHYSICAL HEALTHCARE IN KIDNEY TRANSPLANT PATIENTS: PSYCHOLOGICAL WELLBEING AND HEALTH BELIEFS ABOUT IMMUNOSUPPRESSION MEDICATION

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Background: An increased prevalence of depression and anxiety in long-term (>7 years) kidney transplant patients (LKT) has been associated with medication non-adherence and poorer transplant outcomes. Integrating physical and mental health care is a key national priority in the UK and a screening package has been developed to facilitate this through collection of patient reported data. We have previously identified and reported significant

psychological morbidity in LKT. In this pilot study we investigated health beliefs of LKT on their immunosuppression medication (IS).
Methods: Between 01/09/16 and 30/11/16 all LKT attending our Transplant clinic were screened using (i) Patient Health Questionnaire (PHQ-9) (ii) Generalised Anxiety Disorder Questionnaire (GAD-7) and (iii) Renal Health Beliefs Questionnaire (RHBQ).
Results: $N = 50$ LKT were screened. Their mean age was 53.1 years (range 22–80 years). 49% were female. 44 patients reported symptoms of depression. Of those 30 (68.2%) had mild symptoms, 10 (22.7%) had moderate symptoms and 4 (9.1%) had moderately severe depression. 12 patients reported symptoms of anxiety. Of those 6 (50%) had probable generalized anxiety disorder. 24 (48%) patients reported the health of their kidney significantly affected their lives. 15 (30%) reported little or no control over their risk of kidney transplant failure. All patients reported that IS interfered with their lives. 47 (94%) agreed their health depended on these medications. 16 (30%) patients reported unpleasant side-effects. Only 8 (16%) patients avoid using IS, however 34 (68%) regularly forget to take IS.
Conclusion: Our results demonstrate significant psychological morbidity in LKT. General understanding about the importance of IS in this cohort was good, however a significant proportion are non-adherent. Analyses to identify associations between physical and mental health parameters on medication adherence are underway and will inform targeted treatment to improve adherence.

Basic Ethics/law/psychosocial/public policy Donation and donor types

BO081 FAMILY APPROACH IN EMERGENCY CLINICAL COUNTY HOSPITAL OF ORADEA FOR ORGAN AND TISSUE DONATION

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Background: This retrospective study shows particularities in the psychologies of different families of identified potential donors within the January 2008 – December 2016 period, depending on a case-by-case basis on the personal religion of the families.
Material and Method: 465 potential donors were identified, of which 286 were considered eligible. The ineligible donors were declared as such because of hemodynamic instability, the presence of viral infections with Hepatitis B or C, syphilis, neoplasms or forensic dismissals. In Oradea, 30% of families refused organ donation, compared to the alarming overall country-wide refusal rate of over 60%.
Motives:

- 24% are presumed objections of the potential donors
- 24% refusal of closest next-of-kin
- 12% not knowing the thoughts of the donor
- 11% not understanding the concept of cerebral death
- 8% concerns regarding to the esthetics of the body post-donation
- 7% problems with the healthcare system
- 6% social problems
- 2% religious problems
- 1% wishing to take the patient home
- 5% clear dismissal with no declared basis

Results: The determining factors in refusal can sometimes be the misunderstanding of the concept of cerebral death, the feeling that the medical treatment was badly implemented, the poor choice of location where the family was informed and the relationship between the transplant coordinator and the family. Other variables which contribute to refusal are as follows: duration of hospital stay, age of the deceased, socio-cultural level of the family, a certain religious orientation or the absence of family.
Conclusions: We have undertaken a religion-based statistic of families which have agreed to organ donation, with the first place being occupied by families belonging to the reformed cult with 32%, followed by Catholics with 21%, eastern-orthodox families with 18%, neo-Protestants with 3% and other religions with 2% (Jehovah's Witnesses, Jews, Muslims, Buddhists). Religion is an important factor for final consent.

Clinical Ethics/law/psychosocial/public policy Donation and donor types

BO082 RAISING AWARENESS OF UNSPECIFIED LIVE KIDNEY DONATION: AN ELPAT VIEW

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LDKT is the preferred treatment for ESRD patients and unspecified live kidney donation (UKD) is morally justified. Despite excellent outcomes, UKD is limited in Europe for legal and moral reasons and its contribution is under-valued with significant variations in practice and approach. Where UKD is practised routinely, an increasing number of patients in the domino paired exchange programme are successfully transplanted when a 'chain' of transplants is triggered by a single UKD. Our Working Group has examined the limitations on UKD and recommends strategies to increase transplant opportunities by raising awareness and engaging with key audiences across nations including the public, healthcare professionals, policy makers and society leaders. Their roles and responsibilities are defined and discussed in the context of the following recommendations: (i) countries wishing to undertake UKD must have a legal framework to support LOD and be committed to LDKT and UKD; (ii) UKD offers the best opportunity to maximise transplant opportunities for patients with ESRD through the domino paired exchange (donor chains) programme; (iii) raising awareness by providing stratified information that is country specific, culturally sensitive and relevant across all sectors of society offers a sustainable option for increasing UKD activity; (iv) the content and context of raising awareness initiatives must be relevant for both mature and emerging programmes and all target audiences; (v) collaboration between dedicated groups: previous UKDs, healthcare professionals and procurement organisations, is the most effective model for engaging with target audiences; (vi) competent authorities with support of dedicated groups are best placed to achieve legislative change in individual countries. Increasing UKD by raising awareness contributes more kidneys to the shared living donor pool, extending the benefit of LDKT to more patients, even if they do not have a suitable living donor of their own.

Basic Kidney Immunosuppressive agents

BOS84 DIFFERENTIAL EFFECTS OF IMMUNOSUPPRESSIVE DRUGS ON DNA METHYLATION IN T CELLS

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The immune response after transplantation can be affected by DNA methylation – an epigenetic modification that regulates gene expression. We wanted to know whether immunosuppressive drugs might control T cell function via changes in DNA methylation. In activated T cells, we determined the effects of tacrolimus and mycophenolic acid (MPA) on DNA methylation of the promoter region of interferon-gamma (IFN-γ) – a pro-inflammatory cytokine.

Naive T cells (CCR7+CD45RO–) and memory T cells (CD45RO+ and CCR7-CD45RO-) isolated from healthy donors were stimulated for 3 days with α-CD3/CD28 with or without tacrolimus (10 ng/ml) or MPA (0.2 μg/ml). DNA methylation was quantified by pyrosequencing at two CpG sites (CpG-54 and CpG-186) in the *IFN-γ* promoter. T cell differentiation and IFN-γ protein production were analyzed by flow cytometry.

After stimulation, naive T cells differentiated into a memory-like phenotype (CD45RO+) and this differentiation was inhibited by tacrolimus and MPA ($p = 0.02$). In terms of *IFN-γ* DNA methylation, the average percentage at the two sites decreased in naive T cells from 79.3% to 69.8% ($p = 0.002$) after stimulation. The two immunosuppressive drugs had different effects on this reduction in DNA methylation. While tacrolimus had no effect, MPA neutralized the effect of stimulation (80.7% before, and 78.2% after stimulation). In memory T cells, DNA methylation and differentiation were unaffected by the immunosuppressive drugs. IFN-γ protein production by the memory cells on day 1 was blocked by tacrolimus but not by MPA.

In stimulated T cells, *IFN-γ* DNA methylation was affected by MPA but not by tacrolimus, while T cell differentiation was inhibited by both immunosuppressive drugs. These results suggest that these drugs induce changes in DNA methylation independently of changes in cell phenotype. Therefore we conclude that differentiation and DNA methylation follow different dynamics after immune activation of T cells.

BOS85 IMPACT OF MYCOPHENOLIC ACID ON T-CELL METABOLIC REPROGRAMMING

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Naïve and memory T cells rely on oxidative phosphorylation but activated T cells use anaerobic glycolysis to support rapid cell growth and proliferation. This metabolic shift is critical for T cell fate and polarization, and is regulated by metabolic checkpoints, including Myc, HIF-1α, AMPK and mTOR. Our objective was to determine the impact of mycophenolic acid (MPA), compared with rapamycin (Rapa), a classic inhibitor of the metabolic checkpoint mTORC1, used as a control, on proliferating T cell metabolism.

In vitro experiments were performed on the Jurkat T cell line incubated with MPA and Rapa from 24 to 72 h. We used RT-PCR, Western Blot, glucose uptake, glycolytic and glutaminolytic flux experiments and lactate and ATP dosage.

We identified a drug-specific transcriptomic signature of key enzymes and transporters involved in glycolysis, glutaminolysis or nucleotide synthesis, resulting from significantly different effects on metabolic reprogramming. MPA produced an early and transient drop in intracellular ATP content related to the inhibition of the *de novo* synthesis of purines, leading to the activation of the energetic sensor AMPK. The analysis of glycolytic or glutaminolytic fluxes indicates that both MPA and Rapa produce a significant decrease of glucolytic flux, in agreement with a reduction in glucose uptake, both also in glutamine oxidation. In addition, both drugs reduce aerobic glycolysis. Consistent with this, the expression HIF-1α and Myc, promoting the activation of glycolysis and glutaminolysis, was inhibited by MPA and Rapa.

In conclusion, we report for the first time that MPA profoundly impacts the cellular metabolism of proliferating T cells by generating an energetic distress, decreasing the glycolytic and glutaminolytic fluxes and by targeting the metabolic checkpoints HIF-1α and Myc. These findings open interesting perspectives for new therapeutic targets blocking metabolic checkpoints to inhibit T-cell proliferation.

Clinical Kidney Immunosuppressive agents

BOS87 DIFFERENT REGULATORY EFFECTS OF TACROLIMUS AND SIROLIMUS ON TFH AND TFR IN ALLO-RENAL RECIPIENTS

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Background: Tacrolimus (Tac) and Sirolimus (SRL) are commonly used immunosuppressive agents in renal transplant recipients. T follicular helper cells (Tfh) and T follicular regulatory cells (Tfr) are CD4+T cells subsets which play counter roles in regulating B cells and are reported to be closely related to antibody-mediated rejection (ABMR). However, how do Tac and SRL impact Tfh and Tfr in allo-renal recipients (RTs) remains unclear. Here we investigated the phenotypic and functional variation of Tfh and Tfr in RTs receiving Tac or SRL treatments.
Methods: The frequency of circulating Tfh and Tfr and the expression of Tfh related molecules including inducible costimulatory molecule (ICOS), programmed cell death protein 1 (PD-1) and interleukin-21 (IL-21) were analyzed by flow cytometry in 31 living related RTs treated with Tacrolimus-based regimen (Tac-group), 20 with Sirolimus-based regimen (SRL-group) and 20 healthy volunteers (HC group).
Results: The percentage of peripheral Tfh and the expression of PD-1 on Tfh cells were significantly higher in Tac group when compared with both SRL and HC groups (Fig. A and B). Whereas, no significant difference was found among three groups in regards to IL-21 and ICOS expressions of Tfh. The number of Tfr cells was significantly elevated in FK506 group compared with that in HC group, instead of SRL group (Fig. C). The ratio of Tfh to Tfr in Tac group an SRL group remained comparable to that of HC group. (Fig. D).
Conclusions: Our data showed that the quantity of circulating Tfh with normal IL-21 secreting function was significantly elevated in Tac treated RTs while in SRL treated RTs that remained comparable to HC group. This indicates SRL can suppress Tfh more effectively than Tac, which is crucial in preventing antibody-mediated rejection (ABMR) and maintaining the immune tolerance in renal transplant recipients.

Basic Kidney Immunosuppressive agents

BOS88 EFFECT OF INDUCTION THERAPY REGIMENS ON MONOCYTIC MYELOID-DERIVED SUPPRESSOR CELLS IN KIDNEY TRANSPLANTATION RECIPIENTS

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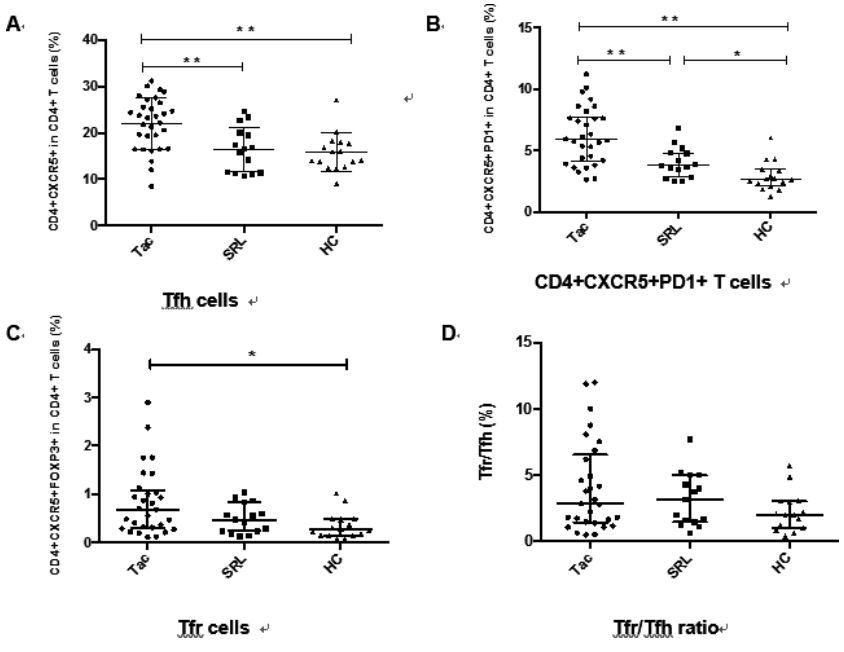
Objective: To investigate the effects of commonly used inductive agents on peripheral blood monocytic myeloid-derived suppressor cells (M-MDSCs) in renal transplantation recipients and to discuss their associated mechanism.
Method: The enrolled patients received rabbit anti-thymocyte globulin (rATG) or basiliximab for induction therapy, with the maintenance immunosuppressive regimen of tacrolimus, mycophenolic acid/mycophenolate mofetil and steroid. CD11b+CD33+HLA-DR-CD14+CD15- M-MDSCs numbers and cytokine levels in peripheral blood, including interferon-γ (IFN-γ), interleukin-2 (IL-2), IL-4 and IL-6, were measured by flow cytometry before the operation and 1 week, 2 weeks, 1 month, 2 months, 3 months afterward.
Result: A total of 47 recipients (rATG 29, basiliximab 18) were included in this study. Compared to the patients with basiliximab, a significant increase of the frequency of M-MDSCs was observed in the rATG group at post-2 month



(rATG group 5.5 ± 2.8% vs. basiliximab group 3.8 ± 1.6%, $P < 0.001$) and post-3 month (rATG group 7.0 ± 3.1% vs. basiliximab group 4.1 ± 2.3%, $P < 0.001$), while there was no difference of the cell numbers between the two groups. In the cytokine detection, levels of IL-2 and IL-4 of the rATG-treated recipients were significantly higher at post-2 week (PIL-2 = 0.032, PIL-4 = 0.019) and post-1 month (PIL-2 = 0.024, PIL-4 < 0.001) than the basiliximab group.
Conclusion: rATG promotes the expansion of M-MDSCs, which is associated with the secretion of IL-2 and IL-4 due to the lymphocytes depletion. The synergistic immunosuppressive effect may contribute to the induction of immune tolerance.

BOS89 CYCLOSPORINE A, BUT NOT TACROLIMUS, INHIBITS THE SERUM RESPONSIVE PATHWAY OF PROXIMAL TUBULAR CELLS THROUGH COFILIN INHIBITION AND REORGANIZATION OF F-ACTIN BRANCHED MESHWORK

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Background: Calcineurin Inhibitors, Cyclosporine A (CsA) and Tacrolimus (Tac), are the keystones of immunosuppressive regimens in solid organ transplantation. However, they induce a nephrotoxicity whose mechanisms remain widely elusive. CsA was previously shown to affect actin organization in podocytes. We explored if CsA and Tac had similar cytoskeletal effects on proximal tubular cells, and the downstream consequences of this reorganization.
Methods: Porcine proximal tubular LLC PK-1 cells were exposed for 24 h to CsA, Tac and VIVIT a specific NFAT inhibitor. LLC PK-1 proteome was analyzed with iTRAQ shotgun proteomics by nano-LC-QTOF tandem mass spectrometry. Actin cytoskeleton was characterized by TRITC-phalloidin labeling of F-actin. Serum response factor (SRF) activity was assessed by luciferase gene reporter assay.
Results: CsA (5 μM) induced a decrease in perimembranous branched F-actin meshwork with a significant decrease in F-actin fluorescence positive area (−3.3%, $p < 0.0001$). This reorganization led to a rigidified aspect of plasma membrane of proximal tubular cells, which lose their crenelated aspect. On contrary to CsA, Tac and VIVIT had no effect on F-actin area. iTRAQ analysis showed that CsA induced a decrease in F-Actin/G-Actin ratio resulting from a decrease in cofilin/actin ratio. This decrease in F-actin/G-actin ratio induced a MRTF/G-actin cytoplasmic sequestration, leading to SRF inhibition (−56.2% of control activity). Cofilin phosphorylation inhibitor S3-R, which has no significant impact on F-Actin/G-Actin ratio or SRF, blocked CsA effects on actin organization and SRF activity.
Conclusion: Our results suggest that CsA deeply affects the actin cytoskeleton of proximal tubular cells through the inhibition of the severing/nucleating activity of cofilin. This reorganization of actin cytoskeleton leads to G-Actin increase and SRF inhibition. Inhibition of the SRF pathway may trigger tubular atrophy, one of the typical lesions of CsA toxicity.

Clinical Others Immunosuppressive agents

BOS90 PRE-CUT DRIED BLOOD SPOT USED AS STRATEGY FOR THERAPEUTIC DRUG MONITORING OF TACROLIMUS

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Background: Since the introduction of liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS), dried blood spot sampling become a promising strategy for therapeutic drug monitoring of tacrolimus (TaC). However, hematocrit (HT) is currently identified as the most important parameter which could impact on the validity of the results. To solve this problem, we validated a LC-MS/MS method to quantify TaC using an alternative sampling strategy, called pre-cut dried blood spot (PCDBS).
Methods/Materials: 12 μl of EDTA blood samples, calibrators or quality control materials (QCs) (provided by the Waters MassTrak Immunosuppressants XE Kit) were pipetted on 6 mm pre-cut Whatman 903 paper punches. Experiments were performed on a Waters Xevo TQ-S triple quadrupole MS/MS system, with a Waters Acquity UPLC H-Class system. The punching machine was a Perkin Elmer Wallac DBS puncher.
Results: The linear range was between 1.1 and 29.6 ng/ml. The limit of quantification was 1.1 ng/ml. Intra and inter assay precision and accuracy were performed using 4 levels of QCs materials. In all the cases, CV% was minor than 12 and BIAS% was minor than 8. Recovery was between 100% and 106%. QCs were stable for 14 days at room temperature. 91 transplanted patient samples were assayed for TaC in whole blood over a range of 1.2 to 20.1 ng/ml. HT values were between 18.7% and 51.7%. Comparison with PCDBS analysis using paired samples yielded a correlation (R^2) of 0.97 (regression line; $y = 1.09x–0.05$) and a Lin concordance coefficient (ρ) of 0.94. Concordance was also demonstrated using Bland and Altman graphical analysis.
Conclusion: the method is suitable for the intended purpose. Compared with conventional whole blood analysis, PCDBS shows distinct advantages including longer lifespan of samples and easy shipment and storage. This methodology is especially interesting for outpatients, who usually need to travel to the hospital on a regular basis to have their blood samples taken and analyzed.

Basic Kidney Immunosuppressive agents

BOS91 ASSOCIATION BETWEEN TPMT460 G>A AND TPMT719 A>G (POLYMORPHISMS OF TPMT GENE), UGT-275 T>A AND UGT-2157 C>T (POLYMORPHISMS OF UGT1A9) AND THE RESPONSE TO IMMUNOSUPPRESSANTS

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Introduction: in this article, we discuss the use of mycophenolate mofetil and azathioprine in the context of renal transplantation. The objectives of this study were to determine: (i) the impact of two polymorphisms affecting the UGT1A9 gene (UGT-2157C>T and UGT-275 T>A) on the pharmacokinetics and tolerability of MMF; and (ii) the association between two other polymorphisms affecting the TPMT gene (TPMT 460 G>T and TPMT 719A>G) and the toxicity of Azathioprine.
Methods: We studied 94 patients with renal transplants. We used PCR-RFLP technique to genotype the studied polymorphisms.
Results: The frequencies of the mutated allele of UGT-2157C> T (rs17868320) and UGT-2157C> T (rs6714486) were respectively, 0.037 and 0.15. The frequencies of the mutated allele of TPMT 460 G>T (rs1800460) and TPMT 719A>G (rs1142345) were about, respectively, 0.028 and 0.013. It seems that the UGT polymorphism-275 T>A is associated with the onset of chronic rejection in patients with the mutated allele after renal transplantation. However, we did not find any association of these polymorphisms (UGT-2157C>T and CGU-275 T>A) with the tolerance of the MMF. As for the impact of UGT1A9 polymorphisms on the AUC of MMF, we noted that the AUC is reduced in patients carrying the mutated allele of the UGT polymorphism-275 T>A. The association between polymorphisms of TPMT (TPMT 460G>T and TPMT 719 A>G) with AZT toxicity has not been established given the small sample size of patients under this treatment.
Conclusions: A larger sample is required to confirm these results in order to establish these genetic tests as routine pre-transplantation tests to select the adequate treatment and dosing.

BOS92 ASSOCIATION BETWEEN UGT-275 T>A AND UGT-2157 C>T (POLYMORPHISMS OF UGT1A9 GENE) AND THE RESPONSE TO MYCOPHENOLATE MOFETIL

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Pharmacogenomics can provide a better understanding of the mechanisms involved in therapeutic efficacy and the development of adverse effects. It is proposed in this work to determine the relationship between the response to MMF and the polymorphisms affecting the genes encoding the UGT enzyme (UGT-2157 C>T (rs17868320), UGT-275 T>A (rs6711486) to individualize therapy on a genetic basis. The study population included 97 renal transplant recipients. The sex ratio is 1.6. The average age of renal transplant recipients is 29 years. Hemodialysis is the most frequent mode of extrarenal treatment 73.2%. These were related living donors in 63.9%. Patients are under Tacrolimus + MMF in 62.9%. The most frequent infections after renal transplantation are due to CMV in 14.4%. Nephrotoxicity and diarrhea are the most frequent complications with 34% and 54.6%, respectively. It appears that the UGT-275 T>A polymorphism (rs6711486) is associated with a higher frequency of chronic rejection in patients with the mutated allele after renal transplantation. However, there was no significant association between these polymorphisms and the tolerance of MMF which suggests the involvement of another pathway in the occurrence of adverse effects of this drug. The AUC of MMF is reduced in the carriers of the mutated allele of the UGT-275 T>A polymorphism (rs6711486) significantly in the study population. This effect is more pronounced in patients with the mutated allele of UGT-275 T>A (rs6711486) receiving the combination MMF + Ciclosporin compared to those receiving the MMF + Tacrolimus combination. This may be due to the inhibition

of the enterohepatic cycle of MMF by ciclosporin further reducing its availability in the bloodstream. Several studies concluded an effect of this variant on the pharmacokinetics of MMF, it appears tobe a promising candidate for future studies to identify factors modifying pharmacokinetics and the therapeutic response to this drug.

Clinical Kidney Immunosuppressive agents

BOS93 A CYP3A5 GENOTYPE-BASED STRATEGY USING EXTENDED-RELEASE TACROLIMUS IN DE NOVO KIDNEY TRANSPLANTS

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Background: Kidney transplant recipients with the CYP3A5*1 allele (enzyme expressers) reportedly required higher extended-release tacrolimus (ERTAC) doses than those without this allele (nonexpressers) to establish an optimal drug concentration. Moreover, we have reported that blood concentrations showed great variation and could not be controlled exactly during 1 week after transplantation. Therefore, fixing the dose of ERTAC according to CYP3A5 single nucleotide variation during the early post-transplantation period could be a useful strategy for kidney transplantation.
Methods: Thirty-eight de novo kidney transplant recipients were retrospectively divided into two groups: the conventional group (CG, $n = 10$) and the genotype-based group (GG, $n = 28$). The initial immunosuppressive regimen consisted of ERTAC, mycophenolate mofetil, methylprednisolone, and basiliximab. In the CG, ERTAC was initially administered at 0.10 mg/kg/day, regardless of the CYP3A5 genotype and was then adjusted after transplantation to achieve the target trough level (6–10 ng/ml). In the GG, the initial dose was set according to the CYP3A5 genotype (0.15 and 0.10 mg/kg/day for expressers and nonexpressers, respectively). Dose adjustment was not performed until 7 days after transplantation unless the trough level exceeded the permissible range (5–15 ng/ml). Dose adjustments were then performed.
Results: For the GG, 78.6% of patients reached the target trough level of TAC at 14 days after transplantation; 25% of these patients did not require changes to their ERTAC doses. In contrast, for the CG, although 50.0% of patients archived the target trough level, all patients changed their doses. The mean number of dose changes was significantly lower in the GG than in the CG. Adverse events and graft function during 2 months after transplantation were similar between groups.
Conclusion: ERTAC dosing based on CYP3A5 genotyping could facilitate immunosuppressive therapy in kidney transplantation.

		Genotype-based ($n = 28$)	Conventional ($n = 10$)	p value
POD 7	Within therapeutic range	10 (35.7%)	3 (30.0%)	n.s.
	Supra-therapeutic range	1 (3.6%)	1 (10.0%)	n.s.
	Infra-therapeutic range	16 (57.1%)	6 (60.0%)	n.s.
	No dose change	19 (67.9%)	0 (0.0%)	<0.001
	Serum creatinine (mg/dl)	1.30 ± 0.54	1.27 ± 0.29	n.s.
POD 14	Within therapeutic range	22 (78.6%)	5 (50.0%)	n.s.
	Supra-therapeutic range	1 (3.6%)	0 (0.0%)	n.s.
	Infra-therapeutic range	5 (17.9%)	5 (50.0%)	n.s.
	No dose change	7 (25.0%)	0 (0.0%)	n.s.
	Number of dose changes	1.7 ± 1.6	3.8 ± 2.2	0.003
	Serum creatinine (mg/dl)	1.21 ± 0.41	1.18 ± 0.30	n.s.
Adverse events (during 2 months)	Acute rejection	AMR 1 (3.6%)	0 (0.0%)	n.s.
	Graft loss	0 (0.0%)	0 (0.0%)	n.s.
	CMV infection	Antigenemia 8 (28.6%)	Antigenemia 4 (40.0%)	n.s.
	Slow graft function	1 (3.6%)	0 (0.0%)	n.s.

BOS94 EARLY INTRA-INDIVIDUAL VARIABILITY IN TACROLIMUS TROUGH CONCENTRATIONS AND CYP3A5 GENOTYPES IN PEDIATRIC KIDNEY TRANSPLANTATION AND ITS IMPACT ON LONG-TERM OUTCOME

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Background: The individualized approach in immunosuppressive drugs is generally accepted and well-established in adult kidney transplantation (KTP). However, it is under investigated in pediatric population. The goals of this study were to identify whether high intra-individual variability (IIV) in tacrolimus (TAC) can influence on long-term kidney allograft outcome in pediatric field. Furthermore, we hypothesized that cytochrome P450(CYP)3A5 polymorphisms are associated with TAC pharmacokinetics and would thus lead to high IIV.
Methods: We performed retrospective data collections for IIV measurement from pediatric KTP recipients who treated between 2000 and 2010 in Seoul National University Hospital. And we calculate the TAC IIV for one year after the KTP.
Results: A total 142 pediatric patients were identified, and 114 were received TAC-based immunosuppression regimen. Mean follow-up period was 3484 ± 859 days. The patients with higher IIV showed tendency of more acute rejection rate (32.1 vs. 17.2%), BPCAN (25.0 vs. 20.7%) and DSA detection rate (17.9 vs. 13.8%), but statistically nonsignificant ($p = 0.065$, 0.123, and 0.552 respectively). On subanalysis of CYP3A5 of 68 pediatric patients, a 28 CYP3A5 expressers and a 40 nonexpressers were identified. Nonexpressers showed some association with high IIV (65.9 vs. 34.1%, $p = 0.108$), more BPCAN (10.0 vs. 3.6%, $p = 0.642$), more DSA detection rate (25.0 vs. 7.1%, $p = 0.104$), shorter time to detect DSA (74.8 vs. 87.5 months, $p = 674$) and more graft failure rate (7.5 vs. 0%, $p = 263$).
Conclusion: This study shows that IIV has somewhat association with graft outcome in the pediatric KTP setting also. Identification of patients at risk of developing early BPCAN and poor long-term graft survival, through calculate early phase IIV, could improve clinical outcome. Furthermore CYP3A5 polymorphism revealed contribute to high IIV in pediatrics also. Unfortunately, we failed to confirm the statistical significance due to small sample size, but the impact on IIV and graft outcome seemed to stand out.

Translational Liver Immunosuppressive agents

BOS95 INFLUENCE OF DONOR AND RECIPIENT CYP3A5 AND ABCB1 GENETIC POLYMORPHISMS ON TACROLIMUS DOSAGE AND TROUGH LEVEL

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Background: The pharmacokinetic characteristics of tacrolimus (TAC) vary greatly among individuals. Genetic polymorphism of the multiple drug resistance gene-1 (ABCB1) (3435C/T) and the CYP3A5 genes (CYP3A5*1) have the greatest potential to influence the pharmacokinetics of immunosuppressants. The aim of our study was to investigate the impact of ABCB1 and CYP3A5 polymorphisms in both recipient and donor on TAC pharmacokinetics after switching from TAC BID (Prograf®) to TAC OD (Advagraf®) regimen based on a 1:1 mg proportion.
Methods: TAC trough levels and doses required to achieve target blood concentrations, laboratory parameters and metabolic disorders were assessed. Sequencing was applied to detect the SNPs of the specified genes.
Results: We analysed 98 liver transplant recipients, with a median age of 57 years, 36% were females and 16% had HCV infection. The most frequent ABCB1 combination of genotypes was recipient and donor 3435CT (19%). For CYP3A5, the combination CYP3A5*3 in both donor and recipient was the most encountered (25%). The genotype population proportions of ABCB1 showed no statistically significant differences between recipients and donors ($p = 0.48$), but for CYP3A5 the difference was statistically significant ($p = 0.002$). ABCB1 3435CT genotype in both donor and recipient did not influence dosage or trough level of TAC OD. In recipients with CYP3A5*3 genotype who received an allograft with CYP3A5*3 genotype, mean TAC OD dosage requirement was significantly lower at month 1 (3.1 ± 1.2 vs. 4.4±2.6 mg/day, $p = 0.02$) and month 3 (2.9 ± 1.3 vs. 4.2 ± 2.3 mg/day, $p = 0.01$) after switching from TAC BID, but not at month 6 (3.2 ± 1.5 vs. 3.8 ± 1.9 mg/day, $p = 0.27$).
Conclusions: Donor and recipient CYP3A5 genotypes, but not ABCB1 genotypes impact on TAC OD dosage requirements at 1 and 3 months after conversion to TAC OD.

Clinical Liver Immunosuppressive agents

BOS96 ACUTE GRAFT-VS-HOST DISEASE AFTER LIVER TRANSPLANTATION: EXPERIENCE AT A HIGH-VOLUME LIVER TRANSPLANTATION CENTER IN KOREA

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Background: Acute graft-vs-host disease (GVHD) is a rare but life-threatening complication of orthotopic liver transplantation (OLT). We present 6 cases of GVHD after OLT.
Methods: Among our 4294 OLT recipients, we identified 6 patients (0.14%) who were diagnosed with GVHD. Their medical records were reviewed retrospectively.
Results: Liver graft types included deceased donor whole liver graft ($n = 3$) and right liver graft from son ($n = 3$). Mean recipient and donor ages were 57.2 ± 6.6 years and 32.7 ± 10.8 years, respectively. Onset of GVHD symptoms occurred 14 to 32 days after OLT, and initial symptoms were skin rash ($n = 5$) and fever ($n = 1$). GVHD was pathologically confirmed by skin or rectal biopsy. Chimerism of donor lymphocytes was identified in all 3 patients who underwent the short tandem repeat polymerase chain reaction assay. Attempts were made to treat the GVHD in all 6 patients by corticosteroids with or without low-dose calcineurin inhibitor, but we had to stop early or reduce these agents due to aggravation of pancytopenia and septic complications. Ultimately, 5 patients died 6 to 106 days after the onset of GVHD, and only 1 patient recovered. This surviving patient was diagnosed earlier and had been administered the recommended dosage of corticosteroid for a longer period with aggressive infection prophylaxis compared to the other cases.
Conclusions: Because of very poor outcomes of GVHD after OLT, early diagnosis and vigorous treatment should be emphasized, although no effective treatment modality has been established yet. We strongly suggest performing aggressive infection prophylaxis during GVHD treatment.

Clinical Kidney Infection

BOS98 IS CMV PROPHYLAXIS EFFECTIVE IN CMV-SEROPOSITIVE PATIENTS RECEIVING THYMOGLOBULIN AS INDUCTION THERAPY?

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Thymoglobulin (ATG) is considered a risk factor for CMV infection in renal transplantation (RTx). The outcome of our 90-day prophylaxis is not clear. All RTx in CMV-seropositive adults from Jan 10 to Dec 14 with rATG (2–6 mg/kg) as induction therapy ($n = 510$) were evaluated (June 15) using our electronic database. 87 cases were excluded (no clear data, non-renal Tx and graft-loss before day 19). Final analysis included 423 cases with a median f-up of 700 days; initial maintenance IS was tacrolimus/MPA/pred. CMV prophylaxis was defined as at least 14 days of antiviral. CMV disease was diagnosed when clinically suspected plus viremia (PCR or antigenemia) or histology. After a mean of 94 days of prophylaxis, 54 (12.8%) pts developed CMV disease and 369 did not. Patient and graft survival did not differ, but eGFR (MDRD4) at 2 years post-Tx was lower in the CMV group (43 ± 21 vs. 53 ± 21 ml/min, $p = 0.013$). CMV occurred at a later time after RTx (mean 177 ± 85 days), 92% before day 300. 29 CMV cases were syndrome and 25 were invasive disease (24 G-I and 1 encephalitis). Demographics, other Tx features and immunosuppression (3 and 6 months) were similar in both groups except for type of donor and that pts converted to an mTOR inhibitor had less CMV thereafter. CMV pts had lower blood lymphocyte counts at the end of prophylaxis (673 ± 396 vs. 851 ± 562, ROC curve = 690 cells/mm^3, area = 0.596 $p = 0.031$), Acute rejection (AR) occurred more frequently in patients who developed CMV (50% vs. 24.1%, $p < 0.001$). In a multivariate Cox regression model with AR as time-varying covariate, factors associated with subsequent CMV disease were: AR Odds ratio: 2.21 (1.21–4.04), deceased donor 3.43 (1.2–9.8) and mTORi conversion 0.09 (0.01–0.66), controlled for lymphocyte counts. These data indicate that 90-day CMV prophylaxis seems to be effective for prevention of CMV disease in this population, although its incidence is 13% after antiviral withdrawal. Some features could indicate monitoring for late CMV disease.

BOS99 IMPROVED CYTOMEGALOVIRUS VIRAL LOAD PARAMETERS ASSOCIATED WITH EARLIER INITIATION OF PRE-EMPTIVE THERAPY

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Background: Cytomegalovirus (CMV) is an important opportunistic pathogen after solid organ transplant which can be managed by pre-emptive therapy historically initiated when the viral load reaches 3000 genomes/ml (2520 IU/ml). We reasoned that intervention should occur earlier when a seropositive donor transmitted virus to a seronegative recipient (D+R−) to cause primary infection.
Methods: Our standard treatment protocol was changed in July 2012 so that D+R− patients commenced valganciclovir immediately once the viral load exceeded the lower limit of detection of the assay (200 genomes/ml; 168 IU/ml). To facilitate early initiation of therapy in outpatients, D+R− patients were discharged from hospital with a 5-day supply of valganciclovir. Virological outcomes were assessed three years after the protocol was changed, by which time 74 D+R− patients treated under the old protocol could be compared with 97 treated afterwards. The primary outcomes were changes in peak viral load, duration of viraemia and duration of treatment in the D+R− group. The secondary outcome was the proportion of D+R− patients who developed subsequent episodes of viraemia. The treatment protocol remained unchanged for the D+R+ and D−R+ groups who were used as a comparison.
Findings: The median values of peak viral load (27 254 to 6409 genomes/ml, $p < 0.001$), duration of viraemia (43 to 23 days, $p = 0.003$) and duration of treatment (54 to 35 days, $p = 0.004$) were all significantly reduced in the D+R− patients, but not in the other two patient subgroups. Early treatment did not increase subsequent episodes of viraemia.
Interpretation: Pre-emptive therapy initiated at the first sign of viraemia post-transplant significantly reduced the persistence of viraemia, peak viral load and duration of treatment required during follow-up. Widespread introduction of this protocol could reduce the drug exposure and cost associated with pre-emptive therapy.

BOS100 EFFICACY OF EVEROLIMUS CONVERSION FROM MYCOPHENOLATE MOFETIL FOR GANCICLOVIR-RESISTANT CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) infection and disease are major complications in the kidney transplant recipients. Although several clinical studies have indicated that the use of the mammalian target of rapamycin (mTOR) inhibitors may decrease the incidence and severity of CMV infection, efficacy of conversion from mycophenolate mofetil (MMF) to an mTOR inhibitor-based regimen has not been elucidated in patients with ganciclovir-resistant (Gan-R) CMV infection after kidney transplantation.
Methods: Between January 2007 and December 2015, recipients converted from MMF to everolimus (EVR) due to Gan-R CMV infection (EVR-group, $n = 5$) were examined. CMV pp65-antigenemia (C10C11) levels and adverse events were compared between EVR-group and matched historical control group (MMF-group, $n = 31$).
Results: Antigenemia levels of EVR-group were always less than MMF-group. The average period required of intravenous ganciclovir treatment was not significantly different between two groups, but the average period required of oral valganciclovir treatment in EVR-group was apparently shorter than in MMF-group (34 days vs. 70 days). Recurrence of CMV disease after remission occurred in four cases in MMF-group but none in EVR-group. There were no significant differences in adverse events after treatment between two groups.
Conclusion: We recommend switching from MMF to EVR as a useful salvage therapy for kidney transplant recipients with Gan-R CMV infection, when other options are difficult to use for adverse effects or not available (e.g. foscarnet).

BOS101 REDUCTION OF LATE-ONSET CYTOMEGALOVIRUS PRIMARY DISEASE AFTER DISCONTINUATION OF ANTIVIRAL PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS TREATED WITH DE NOVO EVEROLIMUS

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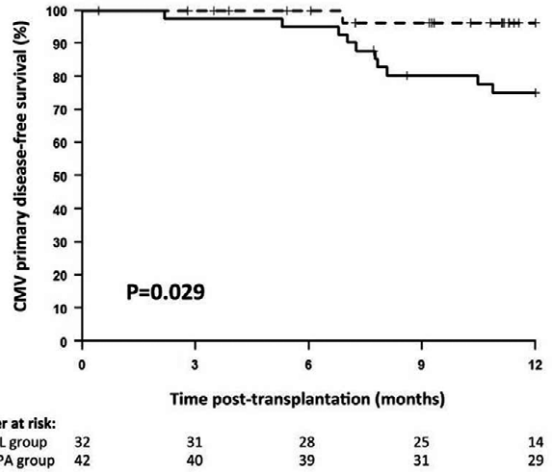
Background: Donor (D)+/recipient (R)− serostatus is critically associated with an higher risk of cytomegalovirus (CMV) infection and disease. Antiviral prophylaxis is conventionally used in such patients, but late-onset CMV infection/disease still occurs after prophylaxis discontinuation.
Method: We retrospectively analyzed data of 215 low immunological risk patients who received kidney transplantation in our center between 2011 and 2016.
Results: Ninety-seven patients received a combination of everolimus (EVL)/reduced doses of calcineurin inhibitors (CNI) (EVL group) *de novo*, and 118 received a combination of mycophenolic acid (MPA)/standard doses of CNI (MPA group) *de novo*. All patients received induction by basiliximab, steroids and standardized antiviral prophylaxis depending on their CMV D/R serostatus. D+/R− recipients comprised 17% (n = 16) of the EVL group and 19% (n = 22) of the MPA group (p = 0.722). In the D+/R− subgroup, the 1-year incidence of late-onset CMV primary disease after the withdrawal of prophylaxis was lower than that in the EVL group (6% vs. 41%, p = 0.025). Kaplan-Meier analysis of 1-year CMV primary disease-free survival in seronegative patients showed significantly better survival in the EVL group (p = 0.029, log-rank test) [figure 1].
Conclusion: The *de novo* use of EVL reduces late-onset CMV primary disease after the withdrawal of antiviral prophylaxis in kidney transplantation patients.

Figure 1 : One-year CMV disease-free survival among CMV-seronegative kidney transplant recipients in the CNI/EVL group (dashed curve) and the CNI/MPA group (solid curve).



Translational Kidney Infection

BOS102 ATG DOES NOT INCREASE CMV INFECTION IN D+R− KIDNEY TRANSPLANT RECIPIENT

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Rabbit-derived anti-thymocyte globulin (rATG) is the most used T-cell depleting agent in solid organ transplantation but has been associated with an increased risk of cancer and infection. However, prospective studies comparing rATG with other induction treatment failed to isolate a clear excess of CMV infection risk with rATG. Heterogeneity of patients in front of the CMV serostatus of donor and recipient, rATG dosages, CMV preventive strategies and absence of lymphocyte kinetics description are potential issues to explain those contradictory results. In this work, our aim was to compare the kinetics of T lymphocyte subsets in a homogeneous retrospective cohort of D+R− kidney transplant patients, receiving either anti-IL2 receptor antibody (anti-IL2RA) or rATG as induction therapy, transplanted between January 2003 and December 2011 with a two-year follow-up post transplantation. Three groups of CMV preventive strategy (preemptive strategy, 3 or 6 months of universal prophylaxis) were individualized. 168 D+R− patients were enrolled, 54 with rATG and 114 with anti-IL2RA. Incidence of CMV infection (55% in anti-IL2RA and 60% in rATG group, p = 0.6) and CMV disease (42% in anti-IL2RA and 50% in rATG group, p = 0.45) were not different between the two groups and in each CMV preventive strategy subgroups. Interestingly, CD4 lymphopenia was associated with CMV infection independently of rATG (p = 0.0001). When the CD4 T cells count was above 368/mm^3, we observed a reduction of the risk of CMV DNAemia more than 5-fold (RR = 5.42, [CI 95% 1.2; 25.6], p = 0.03). Our results suggest that the risk of CMV infection is not increased by rATG, compared to anti-IL2RA in D+R− patients, but is promoted by CD4 lymphopenia.

Clinical Kidney Infection

BOS103 CMV INFECTION IN RENAL TRANSPLANT RECIPIENTS: INCIDENCE AND EFFICACY OF PROPHYLAXIS ACCORDING TO CYTOKINE SINGLE NUCLEOTIDE POLYMORPHISMS

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CMV Infection	OR (CI 95%)	p
pro-IL18 HAPLOTYPE: carriers GC vs no carriers	2.79 (1.01–7.78)	0.044
Acute vascular rejection	2.63 (1.55–4.45)	<0.001
Recipient age: <60 years vs. ≥60 years	1.73 (1.11–2.69)	0.014
Cold ischemia time >18 h vs. ≤18 h	1.64 (1.07–2.50)	0.022
Delayed graft function	1.63 (1.06–2.51)	0.026

Early detection of patients with a higher susceptibility for developing post-transplant viral infections can aid in their prevention.
Objectives: To evaluate the influence of single nucleotide polymorphisms (SNP) of IL10, TNFα, IFNγ and IL18 in the incidence of CMV infection in renal transplant recipients.
Methods: We performed a retrospective cohort study from a prospective database that included 709 patients that received a renal transplant at our center between 2005 and 2013. All patients who had received a previous transplant, were not Caucasian, had primary graft failure or were deceased in the early post-transplant period were excluded. SNP analysis was performed by real-time PCR with TaqMan® probes. The patients were stratified according to the higher producing genotype.
Results: The incidence of CMV infection and disease was of 37% and 6.4% respectively. The main risk factors are described in tables 1 and 2. There was a significant independent association between SNP -137 G/C of IL18 and CMV infection, where carriers of G allele had a higher risk of CMV infection (OR = 2.79; CI 95%: 1.00–7.78; p = 0.044). In the subgroup of patients that received prophylaxis for CMV, the main risk factor for infection after discontinuation of Valganciclovir was being a carrier of G allele (OR = 5.10; CI 95%: 1.12–23.20; p = 0.035). No patients developed CMV disease within non-carriers.
Conclusions: SNP -137G/C of IL18 can affect the incidence of CMV infection and response towards prophylaxis with Valganciclovir. The knowledge of these polymorphisms in recipients previous to transplantation and a closer virological monitorization in those patients with a higher risk of CMV infection can aid in the individualization of treatment regimens and lower the rate of infectious complications.

BOS104 HUMAN LEUKOCYTE ANTIGEN ALLELES AND CYTOMEGALOVIRUS DISEASE IN KIDNEY TRANSPLANT PATIENTS

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Introduction: Cytomegalovirus (CMV) is an important cause of morbidity and mortality in transplant patients. With more patients undergoing transplants, along with the expanding indications for immune-modulating agents, the number of patients at risk for developing CMV disease is increasing.
The Aim: The aim of our study was to analyze the association of CMV disease and particular HLA genotypes in recipients after transplantation.
Material and Methods: This study included 674 kidney transplantations between January 2009 and December 2014 and it was performed in CIURT Cluj-Napoca. The patients were divided into two groups according to the presence of CMV disease. All recipients were serum CMV IgG positive (100%), but none of them was CMV IgM positive (0%).
Results: From a total of 674 patients, 416 patients were male and 258 patients were female. The range of patients was 4–74 years. Relation of each allele to CMV disease is expressed through an OR calculated in the context of all allele at each locus. The HLA alleles frequencies were determined in patients with CMV disease and recipients without CMV disease. The difference in HLA frequencies between these two groups was statistically significant.

Association analysis of HLA-A reveals the A36 allele ($p < 0.05$) predispose to increased risk of CMV disease. The OR values was 18.50. HLA-B with greater allelic polymorphism has two alleles predispose to CMV disease: B48 and B57 shown by $p < 0.05$. Concerning HLA-DRB1, our results reveals one protective allele against developing CMV disease: DRB1*09, $p < 0.05$, and $OR < 1$ and no alleles for this locus which give susceptibility to CMV disease.
Conclusion: We have concluded that a larger number of samples will be required to confirm our data: the association of HLA-A36, HLA-B48, HLA-B57 with CMV disease and HLA-DRB1*09 may be protective against CMV disease.

BOS105 BKV AND CMV COINFECTION IN RENAL TRANSPLANT PATIENTS: RESULTS FROM A LARGE MULTICENTER STUDY

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BK virus (BKV), Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) reactivations are common after kidney transplantation (Tx), and associated with graft failure and increased morbidity and mortality. CMV is a risk factor for BKV and EBV reactivations, but the effects of viral coinfections remain unknown. Here we study the prevalence and clinical implications of the viruses in Tx.

In a large prospective multicenter study, 3797 blood samples from 541 kidney transplant recipients were analyzed for BKV, EBV and CMV load by qPCR. The measurements were performed throughout eight visits during the first post-Tx year. Clinical characteristics, including graft function (GFR) were collected in parallel.

BKV was the most prevalent infection, had the higher viral load and the lowest clearing rates. Patients with BKV or CMV monoinfection over 10 000 copies/ml had a significant renal function impairment 1-year post-Tx compared to non-infected. 115 patients were BKV^+CMV^+; both infections were significantly associated ($p < 0.0001$). The temporal sequence of the two infections was not uniform: 52 patients showed BKV reactivation before CMV, 42 had CMV before BKV and in 21, both were detected simultaneously. Coinfected patients did not have higher viremias than monoinfected and did not show more rejection episodes. Nevertheless, coinfected patients showed a significant loss of renal function comparing to monoinfected infections. Even at much lower thresholds (BKV > 1000 and CMV > 4000) than for monoinfected patients, coinfected patients showed a significant loss of GFR of 10.2 ml/min 1-year post-Tx ($p = 0.03$). For EBV, a significant association ($p = 0.02$) was found with CMV. High peak tacrolimus blood levels were significantly associated with viral reactivation.

Our results demonstrate the significance of BKV and CMV coinfection for the long-term allograft function and highlight the importance of a good therapeutic monitoring and control of the viral reactivations, even at low viremia levels.

BOS106 SCREENING OF POLYOMAVIRUSES VIRURIA IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Infection with human polyomaviruses (PV), such as BK virus (BKV) and JC virus (JCV), are very common, but their clinical meaning are often miscalculated. It's estimated that up to 80% of the population had contact with PV and is seropositive, however polyomavirus-associated nephropathy (PVAN) was mostly described in immunocompromised patients. PVAN is an emerging disease in kidney transplant recipients (KTRs) because of high graft loss up to 80%.
Methods: From November 2015 to February 2017 we examined 91 KTRs. Patients were between 8 day and 16 years after kidney transplantation (KTx). We examined morning urine sample for the occurrence of PV (BKV and JCV) DNA by Quantitative Real-time PCR.
Results: PV viruria has been found in 32.9% of all patients. In the first period after KTx, PV infections were more often caused by JCV than BKV (53.3% vs. 43.7%), but with time BKV participation was increasing.

The presence of symptoms of PV infection (increase of serum creatinine concentration by more than 20% in a period of 3 to 6 month) were noticed in one third of patients from groups B, C and D with confirmed PV viruria. The prevalence of BKV and JCV was similar: 23% of BKV and 19% of JCV infection.

In our study there are no differences in frequency of infection PV depending of regimen of immunosuppressive (IS) maintenance therapy. Although, we have found correlation between applied dose of MMF and risk of infection PV: KTRs with PV viruria took higher dose of MMF than KRTs without this infection (mean daily dose of MMF 1423.07 mg vs. 1063.03 mg, $p = 0.03$).
Conclusions: PV infection is common in patients after KTx, however the symptoms occur in only one third of patients with PV viruria. Screening for urinary PV viral load seems to be necessary thus it will allow early intervention and prevent from loose function of kidney graft due to PVAN. The factor that most strongly impact on the presence of the PV in urine is the dose of antiproliferative agent.

BOS107 POLYOMAVIRUS (BK) MONITORING AND EARLY REDUCTION OF IMMUNOSUPPRESSION REDUCES GRAFT LOSS SECONDARY TO BK VIRUS NEPHROPATHY: SIR PETER MEDAWAR TRANSPLANT UNIT, ROYAL LIVERPOOL UNIVERSITY HOSPITAL

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Background: The BK viremia related renal graft loss is up to 60% before screening. We report the effects of BK monitoring, and modification of immunosuppression on the 5-year allograft survival in patients who developed BK viremia after kidney transplant.
Material and Methods: *Patients*: This was a retrospective study of 101 renal transplant patients in a period of 12 months from April 2011 with a five years follow up. Twenty patients were excluded due to lack of follow-up data. All patients subjected to a screening protocol by measuring quantitative serum BK polymerase chain reaction (PCR) monthly for the first 6 months, and every 3 months up to 2 years after transplant.

Immunosuppression: Forty two patients had Alemtuzumab and 39 patients had basiliximab as induction therapy. Maintenance therapy for all patients was Tacrolimus (TAC) and Mycophenolate Mofetil (MMF). Our protocol is based on steroid avoidance.
Results: Twenty two percent of patients ($n = 18$) had BK viremia. The first peak appearance of BK viremia was seen in 83% ($n = 15$) within the first 18 months of transplant and latent viremia occurred in 17% ($n = 3$) after 36 months of renal transplant. Thirty three percent ($n = 6$) had significant viremia (BK viral load >10 000 copies) and 67% ($n = 12$) had non-significant viremia. Our strategy is to stop MMF, start prednisolone for significant viremia and maintaining TAC level at 4 to 5, while for non-significant viremia close monitoring and reduce MMF on clinical need. The average time to clear significant and non-significant viremia was 16 months vs. 7 months respectively. Clearance achieved in all cases with exception of 3 cases of significant viremia in which 2 cases had not cleared the virus over study period and 1 case died before clearance. Five-year graft survival for those with or without BK viremia was 89% vs. 92% and graft loss 2.4% ($n = 2$) secondary to BK virus nephropathy.
Conclusion: Our BK viremia related renal graft failure after screening was only 11%.

BOS108 LOW-DOSE CIDOFOVIR AND CONVERSION TO MTOR IN POLYOMA VIRUS-ASSOCIATED NEPHROPATHY (PVAN) – A CASE SERIES

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Background: Polyoma virus-associated nephropathy (PVAN) is an emerging disease in renal allograft recipients with a high rate of allograft loss. Overall reduction in immunosuppression is a cornerstone of PVAN therapy, whereas optimal drug combination, as well as specific antiviral therapy remain a question. We report safety, efficacy and outcome data of a protocol using low-dose cidofovir as well as a conversion in the immunosuppressive regimen in a case series of 20 patients with PVAN and progressive renal functional deterioration.
Methods: Patients with biopsy-proven PVAN received single low-dose cidofovir according to the Tübingen Cidofovir Protocol, developed to effectively deliver therapeutic drug concentrations at limited nephrotoxicity and were converted to mTOR-based maintenance immunosuppression. Polyoma virus replication and renal function were prospectively monitored over time.
Results: Results from an ongoing case series (since 2007) of currently 20 patients with a median follow-up of 4.4 [0.4–9.9] yrs. are reported. Median time to PVAN diagnosis was 260 [60–2908] days after transplantation. Median eGFR prior to therapy was 28 [10–48] ml/min/1.73 m^2. The protocol allowed antiviral therapy without adverse nephrotoxicity, irrespective of allograft function. 18/20 pts. were initially converted to mTOR-based immunosuppression, whereas two patients had to discontinue the mTOR due to side effects. 16 patients stabilized allograft function, 4 patients progressed to ESRD due to PVAN, one of which was successfully retransplanted without recurrence. Polyoma virus clearance from plasma was achieved in 80% of patients after a median of 90 [27–298] days.

In conclusion, low-dose cidofovir and conversion to mTOR-based immunosuppression allows for effective virus clearance and preservation of allograft function in a high proportion of patients with PVAN and progressive allograft dysfunction and may prolong allograft survival in these patients.

BOS109 CLINICAL SIGNIFICANCE OF BK VIRUS-SPECIFIC T CELL IMMUNITY MONITORING USING ELISPOT ASSAY IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: BK virus (BKV) is an important opportunistic pathogen which can affect allograft outcome. However, suitable parameters to predict the reactivation and the clearance of BKV are still unclear. This study aimed to investigate whether BKV-specific T-cell immunity measured by an interferon-γ enzyme-linked immunosorbent spot (ELISPOT) assay can predict the outcome of BKV infection.
Methods: We included 50 kidney transplant recipients (KTRs) and 44 healthy controls (HCs). BKV-specific CD4+ T-cell responses for Large T (LT), Small T (ST), VP1, VP2, VP3 antigen were measured by using an ELISPOT and BKV-specific IgG antibodies were measured using ELISA method. Cut off value for positivity of ELISPOT was 10 SFU/106 PBMC. KTRs were divided into three groups according to the real-time PCR-determined BKV status: patients who never had viremia, patients with current viremia and patients who recovered from previous viremia. We compared BKV-specific T cell immunity between KTRs and HCs, and we also investigated whether it is associated with the clearance of BKV or the development of BKV-associated nephropathy (BKVN) in KTRs.
Results: All five BKV-specific T cells significantly increased in KTRs compared to HCs. Among KTRs, patients who recovered from previous viremia tended to have higher ELISPOT results for all antigens than the others. And patients who achieved the clearance of the virus during the study period had a higher T-cell immunity compared to patients with persistent viremia ($p < 0.05$). Of 30 cases of allograft biopsies done after the virus reactivation, BKVN comprised of 16.7%. KTRs with BKVN had poorer T-cell responses to LT, ST, VP1 antigen compared to the patients without BKVN ($p < 0.05$). BKV-specific IgG antibodies had no role in this study.
Conclusions: BKV-specific T cell response measured by ELISPOT may be useful to predict the clearance of viremia and development of BK nephropathy.

Translational Kidney Infection

BOS110 ORIGIN AND PATTERN OF HUMAN POLYOMAVIRUSES REPLICATION AFTER KIDNEY TRANSPLANTATION: A PROSPECTIVE OBSERVATIONAL STUDY

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Background: Human Polyomaviruses (HPyV) are ubiquitous DNA viruses establishing latent infections in the host. Immunosuppression is a recognized risk factor for HPyV reactivation. The most extensively studied HPyV in kidney transplantation (KTx) is BK virus (BKV) but other HPyV such as JC virus (JCV), Merkel Cell PyV (MCPyV), and Polyomavirus 9 (HPyV9) have been detected in KTx. Origin, natural history, and clinical significance of these HPyV remain unclear.
Methods: Urine and blood samples from 22 KTx donor/recipient pairs were collected immediately before KTx and on post KTx day 1 (T1), 15 (T2), 30 (T3), 60 (T4), 90 (T5). Samples were tested for BKV, JCV, MCPyV, Polyomavirus 7 (HPyV7), and HPyV9 genome by virus-specific DNA TaqMan Real Time PCR. Molecular characterization of the amplified viral strains was conducted by automated sequencing.
Results: No HPy vs. viremia was observed whereas HPy vs. viruria was detected in 10/22 (45.5%) donors and 10/22 (45.5%) recipients. Identical HPyV strains were isolated in 6/22 (27.3%) donor/recipient pairs. JCV genome was amplified in 10 donors and in 6 recipients since T1. JCV strains detected in the recipients were identical to those amplified in the paired donors. MCPyV DNA was detected in 3 recipients at T2. BKV genome was detected in 1 recipient at T3. One recipient experienced concomitant replication of JCV and MCPyV. No relationship between HPyV replication and clinical course was identified during the first 3 months of follow up.
Conclusions: Our data confirm that replicating JCV is frequently observed in organ donors. They also suggest that JCV replication in the early post KTx phase is common. We demonstrated that JCV early post KTx infections are caused by viral strains transmitted by the donors. MCPyV and BKV post-transplant replications observed in this series were likely due to reactivation of recipient strains. Extended follow up is needed to rule out clinical impact of early JCV infection after KTx.

BOS111 DNA VIRAL INFECTIONS ASSAY IN KIDNEY TRANSPLANT RECIPIENTS BY A NEW HIGH THROUGHPUT MASS SPECTROMETRY METHOD

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Introduction: Infections represent a major complication after renal transplant with an important impact on allograft survival and outcome. Polyomaviruses (PyVs), a group of small and circular dsDNA viruses, mediate a broad spectrum of diseases in immune-compromised patients. NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) is a key regulator of immune and inflammatory responses and the -94ins/delATTG (rs28362491) polymorphism in the gene promoter has been widely investigated for clinical associations. To date, rs28362491 has been shown to influence the susceptibility to systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease and recently renal transplant rejection.
Materials and Methods: We developed a high throughput mass spectrometry (MS)-based method to detect rs28362491 and 18 Py vs. types. Primer pairs of MS assay were designed within the specific large T antigen genes. Viral and human DNAs were extracted from blood samples of 43 kidney transplant recipients, before and after transplantation.
Results: We analysed the correlation among Py vs. infections, rs28362491 genotype and post-transplant follow up. Five out of the 18 viral types tested were found in the specimens analysed: *BKV, JCV, Merkel cell PyV, Human PyV6 and SV12*. In our cohort, 14 patients showed SV12 infection: 10 cases were -94ins/-94ins, 4 were -94ins/-94del. All the patients with the NF-kB-94del/-94del genotype were characterized by the absence of SV12 strain. No correlation between genotype and viral infection was observed for the other viral types.

Conclusions: Our MS assay improved the Py vs. typing and allowed to drive towards the identification of novel biomarkers for the infective management of transplanted patients. The genetic background might modulate the viral infection susceptibility in renal transplant recipients.

Clinical Kidney Other

BOS112 ASSOCIATION BETWEEN DIPSTICK PROTEINURIA AND ALLOGRAFT OUTCOMES IN LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS

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Background: Proteinuria is one of the important factors suggestive of kidney function impairment. Previous epidemiologic studies had demonstrated that greater than trace amounts of protein on a casual urine dipstick may be an important predictor of long-term clinical outcomes in general population. In kidney transplant (KT) recipients, there were few data concerning it.
Methods: Thus, we retrospectively analyzed 238 living donor KT recipients to investigate impact of dipstick proteinuria on allograft outcomes. All KT recipients were divided into 2 groups according to dipstick proteinuria: control group (n = 190), negative; case group (n = 48), ≥ trace. Cox's proportional hazard model with time-dependent covariates was used to encompass compounding effect of covariates that change over time, including vintage and allograft survival time.
Results: As compared with controls, the change of estimated glomerular filtration rate was prominent in recipients with dipstick proteinuria after 3-year post-KT (−1.5 ± 7.1 vs. −4.4 ± 7.4 ml/min 1.73/m^2/year^1, $p < 0.0174$). In Kaplan–Meier analysis, KT recipients in control group had a better dialysis-free survival as compared with cases (201 ± 6 vs. 164 ± 10 months; log-rank $p = 0.0118$). In Cox proportional hazard models, trace or more dipstick proteinuria was closely associated with long-term allograft loss (HR = 1.964, 95% CI = 1.152–3.348), and further adjustment for age and gender did not attenuated this association (HR = 1.764, 95% CI = 1.050–3.065).
Conclusions: Our results may suggest that presence of small amount protein in urine may be the first sign of deteriorating allograft renal function.

BOS113 DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANTATION: IMPACT ON GRAFT FUNCTION, RENAL TRANSPLANT SURVIVAL AND PATIENT SURVIVAL

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Introduction: Delayed graft function (DGF) is a form of acute renal failure resulting in post-transplantation oliguria, increased allograft immunogenicity. Factors related to the donor and prerenal, renal, or postrenal transplant and factors related to the recipient can contribute to this condition. In renal transplantation, the impact of DGF on prognosis is controversial. We will be interested in the impact of DGF on graft function, graft survival and patient survival.
Methods: One hundred and ninety-one renal transplants performed between November 2007 and June 2016 were analyzed. DGF was diagnosed when serum creatinine levels increased, remained unchanged, or decreased less than 10% per day in five consecutive days in the first week after transplantation.
Results: The mean age of recipients was 33.13 ± 13.04 years. There were 35% females and 65% males.

Univariate analysis revealed the following results. The frequency of DFG was 14.1%. The necessity of hemodialysis was observed in 25.9% (eight cases). DFG occurred in 7.4% cadaveric graft and 92.6% live – graft.

The chronic graft dysfunction was observed in 33.3% of patients with DFG vs. 11.8% of patients without DFG ($p = 0.007$). Acute rejection occured more frequently with DFG (20% vs. 12.8%, $p = 0.27$)

There was a worse graft survival in patients developing DFG but the difference was statistically not significant ($p = 0.052$). Finally we have not fined a real impact on patient survival ($p = 0.69$).
Discussion: Recent studies provide conflicting results. Some centers report DGF as an independent risk factor for acute rejection episodes, reduced long-term graft and patient survival, while others report no impact. This result from differences in definitions (DGF, long-term outcomes), and statistical methods that may partly explain the variability.
Conclusion: DFG can have serious consequences on the long term outcome of renal transplantation.

So, we recommend optimal immunosuppressive regimen for patients with DGF and weekly renal biopsy.

BOS114 THE MANAGEMENT OF RENAL ALLOGRAFT FAILURE

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Background: Management of the recipient with a failing renal allograft is complex. In addition to psychological support, optimisation of immunosuppression and correction of the metabolic consequences of chronic kidney disease (CKD), there should also be timely referral for definitive access or re-transplantation as appropriate.
Methods: We performed a retrospective analysis of all renal allograft failures in a large transplant unit in two recipient cohorts – those whose grafts had failed in the period 1st January 2007–31st December 2011, when all recipients were seen in a general transplant follow up clinic, and those failing between 1st September 2014 and 31st August 2016, following the establishment of a low clearance transplant clinic.

Data was collected from electronic databases and clinical notes.
Results: Grafts failing within one year were excluded from further analysis. There were 52 failures in cohort one (67% male) and 49 failures in cohort two (59% male).

	Cohort one (n = 52)	Cohort two (n = 49)
Age at transplant/graft failure (years, + SD)	41 ± 15/47 ± 16	44 ± 17/54 ± 16
% LD/DBD/DCD	29/69/2	31/49/20
% First transplant	79	84
Cause of graft failure: % CAN/recurrent disease/other	23/17/60	18/16/65
% with history of non-adherence	15	14

Excluding recipients with a rapid and unexpected decline in graft function, 9/20 (45%) patients in cohort one started haemodialysis with a line, despite being known to have declining function with an eGFR of <20 ml/min 6 months prior to graft failure. Only two had been assessed in the vascular access clinic.

In contrast, in cohort two, although 8/24 (33%) predictably progressive patients started dialysis with a line, all had been assessed and offered a fistula.

The rate of pre-emptive listing for a further transplant were similar in both cohorts, despite the second cohort being older at the time of graft failure (54 vs. 47 years), with a greater prevalence of diabetes (22% vs. 12%).
Conclusion: Management of recipients with failing renal allografts in a dedicated low clearance transplant clinic facilitates provision of definitive access prior to return to dialysis, and may improve re-listing prior to graft failure.

BOS115 HYDRATION AND NUTRITIONAL STATUS OF PATIENTS AFTER SUCCESSFUL KIDNEY TRANSPLANTATION

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Background: Hypervolemia is a major risk factor for hypertension leading to cardiovascular diseases and also a frequent problem in patients with chronic kidney disease. Hydration status can be determined by bioimpedance spectroscopy which is a practical, and non-invasive method.

This study was carried out to estimate the hydration and the nutritional status in a cohort of stable kidney recipients (KTRs).
Methods: The study population consisted of 121 patients after kidney transplantation in mean age 51.2 ± 13.5 years. 34% KTRs had diabetes mellitus (DM). Hydration status was assessed through clinical evaluation and bioimpedance spectroscopy over a 24-month observation period. Nutritional status was assessed by clinical (SGA), anthropometric (BMI, body fat, lean body mass contents) and biochemical parameters. eGFR was calculated by CKD EPI formula.
Results: The mean BMI was 25.8 ± 4.1 (range 17.5–39.0); the mean eGFR was 56.4 ± 22.1 ml/min. Nutritional status has not changed during the year. During the study period hydration status assessed by bioimpedance spectroscopy was stable +1.04 ± 2.2 l – at the beginning the study and +0.94 ± 2.3 l – after 24-months. The significant differences in body fat content between patients >60 years. old vs. younger were observed. Elderly KTRs and KTRs with diabetes mellitus presented also, a significantly higher ($p < 0.05$): E/I ratio (external/internal body water), BMI and body fat content. The nutritional status assessed by SGA (DM −5.3 vs. nonDM −6.6 points; $p = 0.0002$) was statistically worse in diabetic KTRs.
Conclusions: The hydration status was at proper range and stable during the observation although extracellular water, E/I ratio and also body fat increased significantly with the age.

BOS116 COMPARISON OF GRAFT FUNCTION AND FACTORS OF INFLUENCE ESTIMATED WITH THREE FORMULAS BASED ON SERUM CREATININE DURING TWELVE MONTHS AFTER TRANSPLANTATION WITH BASIC FUNCTION OF DONATED KIDNEY MEASURED

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Introduction: Assessment of renal function is a crucial component of donor evaluation. The higher measured GFR of donor is independently associated with better allograft outcomes in living donor kidney transplantation. Monitoring graft function and estimation of GFR is recommended method for follow up the patients in post transplant period. The aim of our study is to investigate correlation of directly measured GFR of donated kidney with estimated GFR with the creatinine based formulas and to detect factors of influence on graft function in 12 months after transplantation.
Methods: 50 patients with transplanted kidney from living donor (related and non-related donors) with stabile renal function in period of 12 months after transplantation was included in our study. The mean recipient age was 30.7 ± 9.6 years, and donor age was 55.45 ± 9.41 years. The mean separated directly measured GFR of donated kidney was 47.61 ± 5.72 ml/min. Graft function was estimated on three time points 3, 6 and 12 months with 3 formulas: Cockroft-Gault, MDRD 6 variables and Nankivell.

Direct correlation of estimated GFR with 3 formulas with measured GFR with radiolabeled isotopes 99mTc DTPA was done. Different factors od influence as donor age, time of dialysis treatment and different calcineurin inhibitors as a part of immunosuppression was evaluated.
Results: Estimated GFR at 12 months with MDRD was 72.65 ± 22.6 ml/min, with Cockroft Gault was 94.25 ± 36.42 ml/min, and with Nankivell formula was 81.78 ± 17.89 ml/min. The highest GFR was estimated with C-G formula at three time points. The estimated allograft GFR does not correlated with directly measured GFR of donated kidney. Donor age is most influenced factor on the graft outcomes at 12 months. Allografts from SCD (<60 years) have better function than allografts form ECD (>60 years). The highest estimated GFR was with C-G equation (106.08 ± 39.26 ml/min), and with other formula, Nanki.

BOS117 A CASE DIAGNOSED WITH MITOCHONDRIAL DISEASE AFTER LIVING KIDNEY TRANSPLANTATION

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Case Report: A 30-year-old man was referred to our hospital for living kidney transplantation from his donor who was his father. At the age of 15, he was diagnosed as having proteinuria during a school physical examination. Then, his hearing ability worsened, and he was diagnosed as having sensory hearing loss at the age of 25. At the age of 27, renal dysfunction (serum creatinine level [sCr], 2.17 mg/dl) was diagnosed, and 2 years later, his renal function further declined (sCr level, 4.86 mg/dl). He underwent living kidney transplantation from his donor father at the age of 30.

His family history was significant in that his mother had chronic kidney disease, bilateral sensory hearing loss, diabetes, and dilated cardiomyopathy. Furthermore, many of his relatives had similar multi-organ dysfunction, which was likely to be characteristic of mitochondrial disease. Thus, we first performed genetic testing of his mother, and the results showed mutation of mtDNA (A3243G). Subsequently, we also examined him after kidney transplantation, and we diagnosed him as having inherited mitochondrial disease. He is now 32 years old, and his kidney allograft function and sCr level have been stable for 2 years after transplantation.
Discussion: Kidney transplantation is rarely performed in both adult and pediatric patients with primary mitochondrial disease partly because of the disease severity, especially when it is accompanied by neurologic disorders. Another important reason may be that some patients with this disease are likely to be misdiagnosed because of the wide range of clinical phenotypes. We experienced another patient who underwent living kidney transplantation from his donor sister, and he developed graft failure a few years later. Therefore, transplant teams should be aware of mitochondrial disease as an etiology for kidney failure, and they should consider appropriate consultation, especially for living donor selection, because the disease is inherited from mothers.

BOS118 BUTYRATE PRODUCING SPECIES IN RENAL DISEASE

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Background: End Stage Renal Disease (ESRD) is associated with a decreased intestinal barrier function. This possibly causes bacterial translocation over the intestinal wall, which can trigger a systemic inflammatory response. The cause of this decreased barrier function is not clarified. The permeability or barrier function of the intestine is determined by a family of proteins that form paracellular slit pores called claudins. Butyrate, a short chain fatty acid, facilitates the transcription from the claudins and therefore affects the intestinal permeability. Furthermore butyrate is an important energy source for colon cells. Butyrate is mostly produced through bacterial fermentation of dietary fiber, for which specific bacterial species are required. The most abundant butyrate producing species are *F. prausnitzii* and *Eubacterium rectale*.

The aim of this study is to evaluate whether a depletion of these specific butyrate producing species might be part of the cause of the decreased intestinal barrier function in ESRD.
Methods: We used qPCR to quantify the total amount of bacterial DNA (16S), *F. prausnitzii* and *Eubacterium rectale* in fecal samples obtained from healthy kidney donors, preemptive renal transplant recipients prior transplantation and dialysis patients. We aim to include 20 patients in each group before September 2017.
Results: Median (IQR) copy numbers are displayed in table 1. On group level we found no statistical differences. Individual values are shown in figure 1.
Conclusions: Our preliminary data show that the range in the abundance of *F. prausnitzii* and *Eubacterium rectale* is high. Though there was no statistical difference between the groups, some dialysis patients appeared to have extremely low counts of these specific butyrate producing species. We will continue to include patients in this study to determine if and in which patients a decreased amount of butyrate producing species is present and possibly clinically relevant.

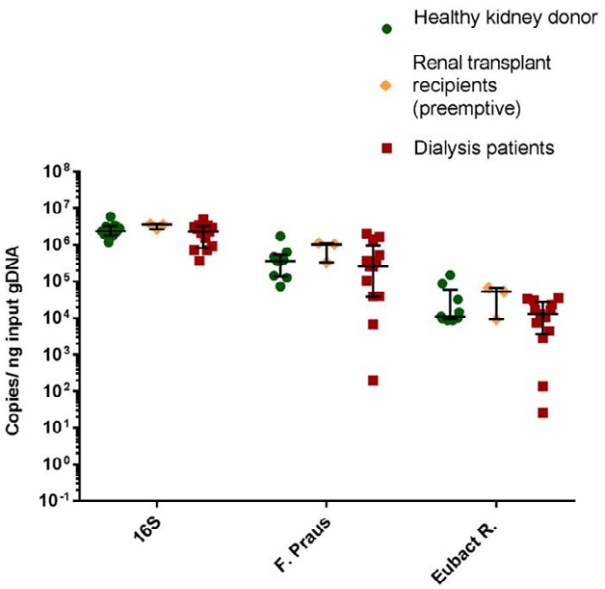

Figure 1. Copies/ng input, median + IQR

	Healthy donors (*n* = 9)	Preemptive (*n* = 3)	Dialysis (*n* = 13)
16S median (IQR)	2 356 883 (1 823 377–3.290 852)	3 571 723 (2 683 784–3 571 723*)	2 311 093 (826 865–3 248 939)
F. prausnitzii median (IQR)	358 169 (135 710–555 506)	1 040 768 (331 288–1 040 768*)	349 171 (349 171–1 417 213)
Eubact. rectale median (IQR)	10 988 (9 287–60. 602)	53 335 (9330–53 335*)	12 896 (3658–20 218)

*50th percentile due to *n* = 3

BOS119 IMPACT OF CALORIE RESTRICTIONS ON THE GLOMERULAR FILTRATION RATE IN KIDNEY TRANSPLANTATION PATIENTS

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Aim: An attempt was made to assess the impact of following a calorie restricted diet on the glomerular filtration rate of kidneys and the nutritional state in the studied group.
Materials and Methodology: Patients with correct body weight and active kidney transplantation of over three months after the transplantation were qualified for the study, whereas patients with diagnosed diabetes mellitus and eating disorders were excluded from it. The patients were divided into two groups: those adhering to a restricted calorie diet (60 patients) and those with no diet (41 patients). The diet consisted of 5 meals a day, with the caloricity for women of approx. 1500 and 2000 kcal in the case of men. The patients ate meat products once a week and were following the diet for approx. 2 months. The control group consisted of patients who did not adhere to any diet.

A body composition analysis was conducted by means of bioelectrical impedance analysis (BIA) and anthropometric measurements. The nutritional state was described using the BMI (body mass index), the waist to height ratio (WHtR) as well as the level of albumin and the Nutritional Index (NI). The excretory function of a transplanted kidney was assessed by calculating the estimated glomerular filtration rate (eGFR) using the MDRD formula.
Results: In patients who followed the restricted calorie diet, which at the same time provided all the necessary building and regulatory components, better glomerular filtration rate was observed compared with patients adhering to the high calorie diet ($p = 0.004$). Hypoalbuminaemia and poor nutritional state ($NI < 1.31$ points) occurred more frequently in persons who did not have any diet ($p = 0.001$).
Conclusions: Rational and balanced diet with restricted calorie intake may have an impact consisting in an improved glomerular filtration rate and better well-being. However, in the case of patients with chronic diseases, supervision of treating physician is necessary.

BOS120 PATIENT SURVIVAL IN KIDNEY TRANSPLANT EXPANDED CRITERIA DONORS: IMPACT OF STEROID WITHDRAWAL

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Steroids are largely effective for the immunosuppressive treatment in renal transplant patients, but cause severe side effects.
Objective: To analyze the effect of steroid withdrawal on patient survival in kidney transplant expanded criteria donors (KTECD)
Material and Methods: A longitudinal, retrospective cohort study, where we included 335 KTECDs performed between February 1999 and December 2011. Factors associated with patient survival were analyzed.
Results: Patient's survival at 2, 5 and 7 years was, respectively, 96%, 88% and 83%. During follow up period (68 months, IR 39-109) 60 patients died (18%). The most frequent cause of death was infectious (27.9%), followed by tumoral (26.2%) and cardiovascular (CVC) (23%).

After performing several models adjusted by age, time on dialysis, cardiovascular disease (CVD), diabetes and propensity scores to receive steroids, Cox's multivariate regression analysis showed in the final model, as risk factors associated to the patient death, the age of the patient (HR 1.1, CI 1.06–1.1, $p < 0.001$) and post-transplant CVD (HR 2.4, CI 1.1–5.2, $p = 0.025$), while the steroid withdrawal was a protective factor (HR 0.2, CI 0.1–0.4, $p < 0.001$).
Conclusions: Steroid withdrawal is a protective factor for the patient death in KTECD. Based on these data, early suspension of steroid therapy could be suggested in this elderly population with low immunological risk.

BOS122 GRAFT LOSS FROM ANTI-GBM NEPHRITIS: A RARE EVENT IN ALPORT SYNDROME EVEN WITH A SEVERE COL4A5/A4/A3 MUTATION

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Background: Alport syndrome (AS) is caused by mutations in α3/α4/α5 (IV) collagen genes, whose severity determines the progression of AS. Post-transplant outcome is good, though anti-GBM nephritis occurs in 3–5% of recipients, clustering in patients with a severe mutation
Aim: To assess whether the severity of the underlying AS mutation affects graft and patient's outcome after transplantation, including the occurrence of anti-GBM nephritis
Methods: Retrospective analysis including AS patients with an identified mutation transplanted between 1972 and 2014. Severe mutations included truncating, splice-site and non-sense mutations. Missense mutations and in-frame deletions were considered non-severe.
Results: 73 patients had received 93 kidney grafts: COL4A5 = 57, COL4A3 = 9, COL4A4 = 6, heterozygous composite COL4A3 and A4 = 1. Forty-one patients had a severe mutation (COL4A5:30, COL4A3:6, COL4A4:5) and 32 had a non-severe mutation (COL4A5:27, COL4A3:4; COL4A4:1). Patient survival was similar in patients with severe and non-severe mutations (89% vs. 84% at 5 years, 83% vs. 75% at 10, 15 and 20 years ($p = 0.46$). Graft survival was not affected by the severity of mutation (77% vs. 63% at 5 years, 60% vs. 55% at 10 years, 55% vs. 55% at 15 years, and 55% vs. 50% at 20 years ($p = 0.65$). Post-transplant cardiovascular, infectious, neoplastic complications and acute rejection rate were similar in both groups. Anti-GBM nephritis occurred in 1 patient with truncating COL4A5 mutation 6 years after transplantation leading rapidly to graft loss. He developed the same episode 3 years after retransplantation. Of 48 grafts biopsies, linear IgG deposits without glomerular lesion were observed in 4 grafts (2 severe COL4A5 mutations, 1 severe COL4A4 mutation, 1 missense COL4A5 mutation).
Conclusion: Anti-GBM nephritis occurred in only 1.4% of AS patients and in 2.4% of the subgroup with a severe mutation which is lower than generally thought. Anti-GBM nephritis may manifest later than previously thought.

BOS123 TREATMENT WITH MYCOPHENOLIC ACID DOES NOT INCREASE MALFORMATIONS IN DESCENDANTS FROM KIDNEY TRANSPLANT RECIPIENTS MALES

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Background: Mycophenolic acid (MA) is prescribed as immunosuppressive treatment after Kidney Transplantation (KT). MA has been associated with teratogenicity in rats and women exposed during pregnancy. Recently, the European Medicines Agency (EMEA) and the Spanish Agency of Medicine and Sanitary Products (AEMPS) warned about the potential teratogenic effects even in descendants of males under treatment with MA, so that contraceptives recommendations should be taken during its consumption. However, there is no available evidence of malformations in the offspring of males exposed to MA. Thus, the aim of the present study was to evaluate the incidence of offspring malformations in KT's male recipients.
Methods: We conducted a longitudinal and retrospective study in which we evaluated the incident of descendants' malformations of 21 KT's male recipients that were under treatment with MA before and at the time of conception.
Results: 28 post-transplant conceptions were identified from 21 KT patients. MA was used as immunosuppressive medication in 25 out of 28 conceptions. Whereas 53.6% ($n = 15$) received Mycophenolate Mofetil, 35.7% ($n = 10$) were under Sodium Mycophenolate. The three remaining patients were under Azathioprine. 11 (58%) patients had had one child, 7 (37%) patients had two children and 1 (5%) patient had conceived 3 children. Mean age of recipients at the time of conception was 36.7 ± 4.7. Median time from grafting to conception was 6 (IQR 2.3–10–7) years. Male or female offspring's gender percentage was comparable. 2 miscarriage episodes were recorded in two different recipients, after which conception was effortlessly accomplished. No malformation was detected among all offspring at birth or after 5 years of age.
Conclusions: In our study, no evidence of MA-associated malformations was observed in descendants of males under treatment with MA. Further research is needed to confirm our findings to properly advice KT recipient males keen to procreate.

BOS124 THE IMPACT ON LONG-TERM KIDNEY FUNCTION OF THE RENAL RESISTIVE INDEX IN THE IMMEDIATE POSTOPERATIVE PERIOD AFTER KIDNEY TRANSPLANTATION: A COHORT ANALYSIS

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Background: The renal resistive index (RI) is a sonographic value that is measured routinely in our hospital in the immediately postoperative period to monitor recipients of a kidney transplantation. We evaluated whether RI measured in the immediate post-transplant phase during ICU admission can be used to predict long-term graft function.

Methods/Materials: The RI was measured by Doppler ultrasonography in kidney graft recipients within the first two days after transplantation between 2005 and 2014. Our primary endpoints were eGFR (CKD-EPI) and mortality at 30 days, 1 year and 5 years. The data were retrospectively retrieved from one tertiary care academic center and 15 peripheral hospitals. Donor, recipient and outcome variables were retrospectively retrieved from the electronic hospital database, the laboratory database, DICOM images, the database on intensive care (Adaptive Server Enterprise), the database of our Transplantation Center, the Eurotransplant database and local databases of peripheral hospitals.
Results: We included 478 patients, with a median age of 54 years (IQR 45–62) and with 295 (61.7%) men. Patients had a median follow-up period of 35 months (IQR 19–59, range 0–127). During follow-up, 30 (6.3%) patients died, of which 27 with a functioning graft. There was no significant correlation between the RI value and the eGFR at 30 days, 1 year, or 5 years posttransplant. However, patients who had died at 1 year and 5 years had a higher RI compared to long-term survivors.
Conclusion: RI, routinely measured the first days after kidney transplantation, has no correlation with long-term kidney function as measured by eGFR, but was associated with all-cause mortality at 30 days, 1 year and 5 years.

BOS125 THE EFFECT ON GRAFT FUNCTION AND SURVIVAL OF BK VIRUS VIREMIA AND NEPHROPATHY IN RENAL TRANSPLANT PATIENTS

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Background: The aim of this study was to evaluate the effects on graft function and survival of BK virus viremia and nephropathy in renal transplant patients.
Methods and Materials: This study included 2575 renal transplant patients who were transplanted from living and cadaveric donors in between 2000–2016 years in our transplant center and divided to two groups. Group 1: BK virus serum PCR negative 2545 patients (male/female: 1716/829, mean ages 38.2 ± 12.4), Group 2: BK virus viremia and/or BKV associated nephropathy (BKVAN: %1.2) 30 patients (male/female: 23/7, mean ages: 40.9 ± 12.6). Tacrolimus, mycophenolic acid derivates (MPA), prednisolone and basiliximab induction therapy were the most used protocols in group 2 (80%). The diagnosis of BKVAN and rejection were confirmed by biopsy. Firstly, dose reduction or end of the MPA (5 patients: %25, 9 patients: %50, 16 patients stop) and than tacrolimus. Secondly, switched to cyclosporine or everolimus. Thirdly, cidofovir use in resistant cases. SPSS 20.0 software program was used for statistical analysis.
Results: Graft survival rates (1./3./5./10. years; %98–90/ %98–80/ %97–80/ 96–80, respectively), were lower in the group 2 (p: 0.003, Figure 1), the rates of acute rejection (16.3–33.3%, p: <0.001), anti-thymocyte globulin uses for rejection (11.9–13.7%, p: <0.001), cytomegalovirus viremia (1–10%, p: 0.004), new onset diabetes after transplantation (11.8–50%, p: <0.001), chronic allograft dysfunction (6.6–46,7%, p: <0.001), serum creatinine levels in last control (1.38 ± 0.9–1.75 ± 0.6, p: <0.001) were higher in the group 2. In 6 graft loss patients (3 BKVAN) were used tacrolimus and MPA based regimen. Serum BKV DNA titers were showed in the Figure 1.
Conclusion: The most effective therapy modalities for BKV viremia and nephropathy according to our study is the reduction or end of MPA and than tacrolimus, switched to cyclosporine or especially everolimus in addition to cidofovir in resistant cases.

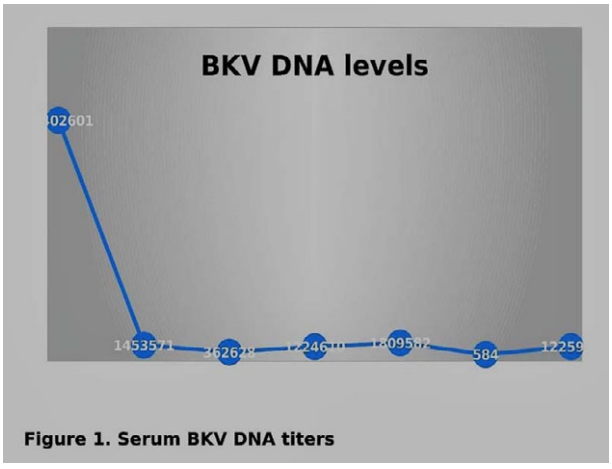

Figure 1. Serum BKV DNA titers

Clinical Liver Other

BOS126 IS SIMULTANEOUS LIVER TRANSPLANTATION (OLTX) COMBINED WITH THORACIC/CARDIAC SURGERY FEASIBLE?

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Background: Experience of simultaneous liver transplant combined with thoracic/cardiac surgery in the UK is extremely limited. There are a number of reasons for this but with continuing improvements in the technical aspects of surgery, immunosuppression/graft survival and post-operative care the indications are likely to expand. We present our experience of simultaneous liver transplants combined with thoracic/cardiac surgery.
Methods: A retrospective review of all such procedures carried out within our unit since 1995 were evaluated from available medical notes and electronic records.
Results: 6 (4M:2F age range 17–56 years) patients underwent combined procedures. A variety of procedures were performed including Simultaneous liver and lung (SiLivLunTx) for cystic fibrosis ($n = 2$), Simultaneous liver and heart (SiLivHTx) ($n = 2$) (for familial hypercholesterolemia $n = 1$ and cardiogenic cirrhosis following a previous Fontan's procedure $n = 1$). A further 2 patients had liver transplantation combined with either an aortic valve replacement ($n = 1$) or CABG ($n = 1$). Two patients received liver re-transplants one for hepatic artery thrombosis at day 6 and another after 14 years for ductopaenic rejection who also required a pacemaker after a cardiac arrest following SiLivHTx. 2 patients required endoscopic management of biliary strictures. Patient mortality at 30 days was 0%. Follow up ranges from 18 months to 20 years during this time 5/6 patients are currently alive and well, one patient who received SiLivCABG died after 8 years due to cardiac complications.
Conclusion: Despite the complexities and considerable risks involved, along with overcoming the logistics of performing 2 major procedures in a single centre, simultaneous liver transplants performed with major thoracic/cardiac procedures including either lung or heart transplantation excellent long-term results can be achieved with zero inpatient mortality even if immediate re-transplantation is needed.

BOS127 COMBINED LIVER AND PANCREATIC ISLETS TRANSPLANTATION – IS IT WORTH IT?

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Introduction: Pancreatic islet transplantation (ILTx) can prevent brittle diabetes (DM) and even achieve insulin independence in some patients. Transplanted islets may be infused into the portal system during liver transplantation (LTx), so combined transplantation carries only small additional risks to LTx. We describe our series of patients with end-stage liver disease and DM who underwent combined LTx + ILTx at our institution.
Methods: From 2/2007 to 7/2014 six patients underwent combined LTx and ILTx. Indications for LTx were liver cirrhosis in 4 patients, neuroendocrine liver metastases and HBV. Indication for ILTx was type 1 DM with zero C-peptide level and secondary DM after total pancreatectomy in 3 cases. Islets were isolated from the same donor and were infused into the portal vein intraoperatively.
Results: The median number of islets transplanted was 244 000 ieq (range 130 000–482 000 ieq, median number 3330 ieq/kg, range 1510–6600 ieq/kg). We observed no complication related to islet infusion. All islets grafts exhibited partial function with median C-peptide and HbA1c levels of 0.27 nmol/l (range 0.05–0.37) and 46 mmol/mol (range 38–57) at 1 year, 0.09 nmol/l (0.02–0.29) and 48 mmol/mol (41–54) at 2 years and 0.08 nmol/l (0.01–0.45) and 55 mmol/mol (43–63) at 3 years. Two patients died after 42 and 46 months (liver retransplantation for ischemic cholangiopathy, tumor recurrence) with partial islets function. Four patients are alive, two with partial islets function (33 and 46 months after ILTx) and two (121 and 115 months after ILTx) with islet graft failed 46 and 65 months after ILTx. No episodes of severe hypoglycemia occurred in any of our patients.

Conclusion: Although we were not able to achieve insulin independence in our small series, partial islets function provided patients with excellent glucose control as shown by HbA1c levels. Adding ILTx to LTx improved quality of life of patients without causing any additional complication.

BOS128 LIVER TRANSPLANT (LTX) IN PATIENTS OVER 65 YEARS OLD: WHERE IS THE PROBLEM? EXPERIENCE OF SINGLE TRANSPLANT CENTER

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Controversial outcomes are reported in the literature on the outcome of LTx in elderly recipients (>65 years old). We aimed to investigate both indications and outcome of LTx in recipients aged 65 to 70 years from 2014 (a time in which the new upper age limit was established) together with early post-transplant Intensive care and hospital stay, and complications at our Ltx Center.
Methods: 17 consecutive over 65 years old transplant recipients (14 Male, 68 median age – range 66–69) (GROUP 1) were compared to 27 consecutive transplanted patients aged 60–64 years (19 Male, 61 median age – range 60–64) (GROUP 2). Baseline features of the two groups were compared by *chi-square* test. Median of hospital stay days as well as complications for each group was collected. Data on overall costs and cost of Intensive Care Unit and High Dependency Care Unit were registered.
Results: No differences were found between GROUP 1 and GROUP 2 on HCV rate at transplant (11 pts vs. 4 pts – p 0.21), ESLD and/or HCC as indication to transplant (48.1% and 44.4% vs. 44.4% and 44.4% respectively– p 0.89), alcohol consumption and smoking history (42.3% and 30.8% vs. 33.3% and 27.8%–p 0.75 and p = 0.83), BMI (25.3 + 3.5 vs. 24.2 + 3.5 mean + SD – p 0.29), Diabetes and Hypertension (30.8% and 30.8% vs. 5.6% and 22.2% – p 0.06 and p = 0.73), renal failure (7.7% vs. 5.6% – p = 1.0), natural MELD score at transplant[14 (11–20) and 15 (13–20) – p = 0.42]. Median post-liver transplant overall hospital stay in GROUP 1 was 40 days (9–73 range) vs. 36 days (13–150 range) in GROUP 2.
Conclusion: In our single centre series the post transplant outcome indicators (post-transplant hospital stay, post-LTx complications and overall costs) of greater than 65 years old recipients are comparable to those younger than 65 years. Aging population leading to an increased number of elderly patients with potential need for transplantation can be faced without affecting cost-efficacy.

BOS129 COST AND RISK FACTOR ANALYSIS FOR PARTICIPATION IN REHABILITATION PROGRAMS AFTER LIVER TRANSPLANTATION

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Background: Ultimately, successful liver transplantation is characterized by complete socio-professional reintegration of the patient into everyday life. Specialized rehabilitation clinics can be of help. The aim of this study is to identify risk factors for participation in rehabilitation programs (RP).
Methods: 182 adult patients after deceased donor liver transplantation were analysed. We used current reimbursement schemes (e.g. G-DRG) and overall drug costs for cost calculation from transplant listing until 3 years post-transplant. Multivariable binary logistic regression analysis was performed to identify risk factors associated with rehabilitation.
Results: 34.1% of patients used an RP with a median duration of 21 (range 5–60) days. Transplant specific independent significant risk factors for participation in RP were the indication acute liver failure (p = 0.001; OR: 8.304 (95%-CI: 2.107–32.730)) and surgical revision due to complications (p = 0.038; OR: 0.474 (95%-CI: 0.232–0.969)). Patients who participated in a RP had a significantly longer graft and overall survival (p < 0.001). Overall mortality rates were 4.8% (RP) and 41.2% (non-RP) (p = <0.001), respectively. In the observed period the total costs did not differ significantly between the groups with and without a RP (p = 0.059; median 168.467€ vs. 213.947€). While the non-RP-group showed significantly higher costs in the first year period post-transplant (p = 0.012), the RP-group showed significantly higher costs in the period 1–3 years after transplantation (p = 0.008).
Conclusion: Participation in RPs is associated with prolonged graft and patient survival. Patients without complications more often participate in RP, especially without the burden of a chronic underlying disease, while patients with post-transplant complications would be expected to benefit more. The higher expenses in the period 1–3 years after transplantation in the RP-group are well explained by overall shorter survival in the non-RP group.

BOS130 LOWER LEVEL OF CARE ADVERSELY IMPACTS THE OUTCOMES OF LIVER TRANSPLANTATION

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Background: Post-transplant care greatly differs across centers and patients. However, the impact of level of care on the outcomes of liver transplantation (LT) is largely unknown.
Materials and Methods: This was a retrospective analysis of adult, de novo LT recipients between January 1996 and December 2015 at a single center. Patients were included if surviving at least 30 days after LT and with one post-transplant outpatient follow-up visit. Levels of care were categorized as follows: LT centers and/or hepatology units at academic hospitals (tertiary, TER); hepatology units at community hospitals (secondary, SEC); non-hepatology units at rural hospitals and/or general physicians (primary, PRI).
Results: Out of 1646 patients undergoing primary LT, 1549 were included (mean (SD) age 50.9 (7.8) years; male 77.6%) and consisted of 673 TER patients (43.4%); 533 SEC (34.4%), and 343 PRI (22.1%). At a mean (SD) follow up of 2871.7 (1869.3) days, 490 patients died (31.6%), 90 (5.8%) were re-transplanted, and 12 (0.7%) were lost to follow-up. Hepatic morbidities accounted for 63.7% of deaths (312/490). Deaths were unevenly distributed across groups: 31.3% (211/673) for TER vs. 26.6% (142/533) for SEC vs. 39.3% (137/343) for PRI (p < 0.0001). Extrahepatic morbidities accounted for 70.1% of deaths in PRI patients (96/137) vs. 30.9% for SEC (34/142) and 22.7% for TER (48/211) (p < 0.0000). Incidence of CKD was numerically higher in PRI patients (76/343, 22.1%) vs. TER (128/673, 19%) and SEC (96/533, 18%) (p = 0.30), but diabetes mellitus (47.8% for PRI vs. 35.8% for SEC vs. 36.9% for TER; p < 0.001) and hypertension (61% vs. 51% vs. 52.9%, for PRI, SEC, and TER patients respectively; p = 0.01) were statistically higher in PRI patients.
Conclusions: Lower level of care is associated with reduced graft survival, higher incidence of extrahepatic mortality, and poorer cardiovascular and glycemic control.

BOS131 IDENTIFYING INDEPENDENT RISK FACTORS FOR GRAFT LOSS AFTER PRIMARY LIVER TRANSPLANTATION

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Background: Hepatic artery thrombosis (HAT) is a dreadful complication after liver transplantation often resulting in graft loss. The aim of this study was to identify independent risk factors for re-transplantation after primary liver transplantation beyond the occurrence of HAT.
Methods: Analyzed were 834 adult patients undergoing primary liver transplantation. A propensity score was developed using multivariable binary logistic regression with HAT as the dependent variable to mitigate differences in patients with and without the onset of HAT. The logit link function of the propensity score was included into multivariable Cox regression analyses for graft loss to adjust the study population.
Results: Graft loss was observed in 143 patients (17.1%). Multivariable Cox regression analysis revealed recipient platelet count (p = 0.045; HR: 1.002; 95%-CI: 1.000–1.003), preoperative portal vein thrombosis (p = 0.01; HR: 1.919; 95%-CI: 1.145–3.080), donor age (p < 0.001; HR: 1.025; 95%-CI: 1.012–1.039), the percentage of macrovesicular steatosis in the donor graft (p = 0.01; HR: 1.041; 95%-CI: 1.015–1.064), early post-transplant complications leading to surgical intervention (p < 0.001; HR: 2.727; 95%-CI: 1.908–3.911), the duration of the transplant procedure in minutes (p < 0.001; HR: 1.005; 95%-CI: 1.002–1.007) as well as the transplantation of a split liver graft (p = 0.01; HR: 2.308; 95%-CI: 1.237–4.137) to be independent risk factors for graft loss. The logit of the propensity score for the adjustment of the occurrence of HAT did not reach statistical significance in the final multivariable Cox regression model (p = 0.13) indicating good adjustment.
Conclusion: Liver transplant programs might benefit from regular donor organ biopsies. Pairing of an elderly donor with a recipient with an elevated platelet count or pre-transplant portal vein thrombosis should be avoided, especially when macrovesicular steatosis is observed or transplantation of a split graft is planned.

Clinical Liver Immunology

BOS132 RISK FACTOR OF ISCHEMIC-TYPE BILIARY LESION AFTER ABO-INCOMPATIBLE LIVING DONOR LIVER TRANSPLANTATION USING B-CELL DEPLETION PROTOCOL

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Aim: To evaluate risk factor of ischemic-type biliary lesion (ITBL) after ABO-incompatible (ABO-I) adult living donor liver transplantation (ALDLT).
Methods: Among 141 ALDLTs performed in our hospital between 2008 and 2014, the clinico-pathological data from consecutive 27 ABO-I ALDLTs were analyzed. All recipients underwent B-cell depletion protocol with preoperative rituximab, plasma exchange (PE), and operative splenectomy. The median follow-up period of the recipients was 26 months.
Results: The median hospital stay after ABO-I ALDLT was 28 days (range: 20–75). The graft function was normalized between POD 12 and 21 after transplantation. All recipients showed satisfactory blood flows of graft's hepatic vein, portal vein, and hepatic artery without stenosis or obstruction on Doppler ultrasound and CT scan. ITBL was developed in 4 recipients (14.8%) between 45 and 112 days after transplantation. The ITBLs were confirmed by the cholangiogram via external biliary stent. One of 4 recipients with ITBL had biopsy-proven AMR prior to development of ITBL; however, three had no evidence of AMR on biopsy. In the risk factor analysis, there was no difference between the patients with ITBL and without ITBL in terms of B-cell and T-cell count, serum titers of isoagglutinin, number of PEs, operative time and transfusion, use of graft infusion therapy, and number of remnant B-cell follicles and plasma cells in the spleen. NK cell counts in perioperative analysis were significantly higher in the patients with ITBL than without ITBL ($p < 0.05$). Preoperative NK cell count >150/μL and postoperative count >120/μL had greater relative risk (RR) for development of ITBL (RR=20 and 14.3, respectively, $p < 0.05$).
Conclusions: High NK cell counts in the recipient's blood could be associated with ITBL after ABO-I ALDLT. Further researches are required to elucidate molecular mechanism of NK cell in the development of ITBL.

BOS133 IS IT SAFE TO USE DCD GRAFTS IN RECIPIENTS WITH PRE-TRANSPLANT PORTAL VEIN THROMBOSIS?

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Patient with pre-transplant portal vein thrombosis (PTPVT) have a higher risk of early mortality and graft loss when transplanted with marginal grafts from donors after brain death (DBD): UNOS data showed that donor risk index (DRI) > 1.7 in these recipients is an increased risk for development of hepatic artery thrombosis (HAT) and primary non function (PNF). The aim of the study is to assess the outcomes of recipients with PTPVT grade I or II transplanted with livers from donors after circulatory death (DCD) compared to DBD. PTPVT was considered a contraindication to DCD liver transplantation at our centre, however some unexpected PTPVT cases were found intraoperatively.

Donor and recipient characteristics were collected from a prospectively held database from 2007 and July 2016 and the outcomes were retrospectively analysed.

Thirty-nine of 347 DCD transplant recipients had PTPVT and were compared with 75 DBD-PTPVT recipients. The median DRI of DCD grafts was greater than DBD livers (2.67 vs. 1.43, $p < 0.01$). Low MELD score and shorter CIT in DCD recipients were part of the centre policy.

Despite a higher peak ALT (894 vs. 297, $p < 0.05$) and AST (966 vs. 158, $p < 0.05$) and greater DGF rate (49% vs. 21%, $p < 0.05$) in DCD compared to DBD recipients, day-7 bilirubin and INR were comparable. The median length of stay in intensive care and in hospital, acute kidney injury and 30-day mortality rates were similar in both groups. PNF/HAT and recurrence of PVT rates were comparable. A greater incidence of ischemic-type biliary lesions incidence was noted in DCD transplants. Patient survival at 1–3 and 5-years in DCD recipients was similar to DBD group (DCD: 79%, 71% and 63% vs. DBD: 92%, 84% and 76%; $p > 0.05$). Similar results were obtained in terms of graft survival.

Selected DCD grafts can be successfully used in recipients with low-grade PTPVT.

Clinical Liver Other

BOS135 CLINICAL OUTCOMES OF OBESE RECIPIENTS (BMI ≥ 30) IN LIVING DONOR LIVER TRANSPLANTATION

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Obese recipients increase difficulty on the aspect of retaining acceptable graft-to-recipient weight ratio (GRWR) in living donor liver transplantation (LDLT). The aim of our study was to assess clinical outcomes of LDLT in obese recipients and to find acceptability in terms of small for size graft (SFSG).

We performed a retrospective study to validate LT outcomes of obese recipients who were defined as body mass index (BMI) ≥ 30 and who underwent LDLT from January 2001 to December 2015 at a single institute. Based on GRWR, obese recipients were divided into Group 1 (GRWR ≤ 0.8) and Group 2 (GRWR > 0.8), and assessed posttransplant study parameters included incidence of early allograft dysfunction, primary nonfunction, and hospital mortality.

61 patients (5.3%) were obese recipients in the middle of 1131 cases who underwent LDLT during the study period. Group 1 included 30 recipients and Group 2 included 31 recipients. In baseline characteristics, there were no significant differences between 2 Groups except for GRWR (0.73 vs. 0.97; $p < 0.001$). Hospital stay after LDLT did not show significant difference between two groups (29 vs. 27 days; $p = 0.217$). In Group 1, hospital mortality was 2 (6.7%) cases, and cause of death was graft dysfunction caused by SFSG and sepsis by pneumonia. In Group 2, hospital mortality were 4 cases (12.9%); 2 cases of primary nonfunction (PNF), 1 case of aspiration pneumonia, and intraabdominal bleeding. In the Kaplan-Meier analysis for graft survival, 10-year graft survival in Group 1 and 2 was 76% and 65%, respectively. LDLT in obese patients represented unfavorable outcomes in terms of postoperative mortality, and graft survival. However, Low graft weight did not impact outcomes after LDLT.

BOS136 IS NASH A SUITABLE INDICATION FOR DCD LIVER TRANSPLANTATION?

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The prevalence of non-alcoholic-steatohepatitis (NASH) is on the increase worldwide. NASH recipients have an increased risk of 30-day-mortality post transplant due to a higher infectious and cardio-vascular complications. In recent years an increasing number of NASH recipients have been transplanted with livers from donors after circulatory death (DCD) in the attempt to reduce waiting list mortality. DCD grafts are though associated with concerns of graft dysfunction and ischaemic-type-biliary-lesions (ITBL). The aim of this study is to analyse the outcome of NASH recipients transplanted with DCD grafts (NASHdcd) compared with those transplanted with livers from donors after brain death (DBD) (NASHdbd).

From a prospectively held database of over 350 DCD liver transplants, 25 consecutive NASH recipients of DCD grafts and 57 patients transplanted with DBD grafts from 2007 and 2015 were included in the analysis. Outcomes evaluated included patient and graft survival, vascular/biliary and renal complications. A multivariate analysis for early–mortality risk was performed.

Donor and recipient characteristics were similar in both groups, a part for an expected lower DRI in NASHdbd. Early mortality rates (respectively 12% vs. 7%, $p > 0.05$), incidence of pre-transplant portal vein thrombosis (16% vs. 16%), long term graft- and patient survival, vascular complications were similar in NASHdcd and NASHdbd, but the ITBL rate was lower in DBD recipients. Univariate analysis showed donor and recipient BMI and MELD scores as risk factors of early-mortality, but the type of graft was not. Regression analysis confirmed both the recipient BMI (OR 1.23; 95% CI 1.01–1.63) and MELD (OR 1.31; 95% CI 1.01–1.27) as independent risk factors of 30-day mortality ($p < 0.05$).

Recipient selection of NASH recipients is necessary for an acceptable outcome. In this context DCD grafts *per se* do not seem to be an additional mortality risk factor for NASH recipients.

BOS137 ENDOSCOPIC MANAGEMENT OF POST-LIVER TRANSPLANT BILIARY COMPLICATIONS: OUTCOME ANALYSIS OF 751 PROCEDURES

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Background: Aim of this study was to assess feasibility, efficacy and safety of endoscopic management of biliary complications at a single center.
Materials and Methods: This was a retrospective analysis of LT patients between January 1996 and August 2016. Patients were enrolled if: adults (≥18 years); recipients of a primary liver graft from deceased donor; undergoing ERCP for biliary complications in the presence of graft vessel patency.
Results: Two-hundred-sixty-nine patients (mean (SD) age 52.5 (8.7) years; male 33.8%) were included. A total of 751 endoscopic procedures were performed with a mean (SD) of 2.8 (2.7) per patient (median (IQR) 1–3). Indications to ERCP were: non-anastomotic biliary strictures (NABS) in 93 patients (34.6%); anastomotic biliary strictures (ABS) in 88 (32.7%); bile leaks (BL) in 41 (15.2%); stones (S) in 29 (10.8%); and varia in 18 (6.5%). Twenty-two procedures (2.9%) failed for technical reasons. Overall treatment-related AEs were observed in 98 procedures (13%) and pancreatitis in 53 (7%), and were fatal in 2 patients (0.7%) (1 pancreatitis, 1 sepsis). A total of 44 patients (16.3%) were referred to surgery or radiological procedures after endoscopy: 16 (5.9%) were re-transplanted (11 NABS; 4 ABS; 1 BL) and 24 (8.9%) underwent hepatico-jejunostomy (12 ABS; 5 BL; 3 NABS; 2 S) combined with liver resection in 2 cases (2 NABS). Four (1.5%) patients required percutaneous radiological treatment (3 NABS, 1 ABS). Patients with NABS had higher number of ERCPs (mean (SD) 4.3 (4.4); median (IQR) 2.5 (2–5); $p < 0.001$) and lower 5-year graft survival rates (71%) vs. ABS (78%), BL (75%), S (78%), and other indications (76%) (log-rank $p < 0.01$).
Conclusions: ERCP shows high feasibility (97.1%) and success (85.2%) rates, with acceptable (13%) post-procedure morbidity and almost nil mortality (0.7%). However, NABS are associated with higher number of procedures per patient ($p < 0.001$) and lower 5-year graft survival rates ($p < 0.01$).

Basic Liver Other

BOS138 THE NOVEL USE BIODEGRADABLE SX-ELLA BILIARY STENT PLACED BY PERCUTANEOUS TRANSHEPATIC APPROACH FOR THE TREATMENT OF BILIARY STENOSIS AFTER LIVER TRANSPLANTATION

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The uncovered self-expandable metal stents placed by percutaneous transhepatic approach (PTA) was used routinely in our center for the treatment of biliary stenosis after liver transplantation (LT). However the rate of complications thereafter achieved more than 60%. Our aim was to evaluate feasibility, safety and outcome of patients treated with biodegradable SX-ELLA biliary stents placed by PTA for the treatment of biliary stenosis after LT in adult and pediatric setting.
Methods: Observational retrospective single-centre study including adult and pediatric patients underwent a first LT who developed biliary stenosis (anastomotic or non anastomotic stenosis) treated with Biodegradable SX-ELLA biliary stents. The median patient follow-up period after stent was placed was 16 months (5–32 months).
Results: Between August 2014 and October 2016 nineteen patients required a biodegradable SX-ELLA biliary stent by PTA. Nine patients were adults with a median age of 61 (49–68) years-old, they received whole graft from brain-dead donors and the biliary reconstruction was end-to-end in all cases. Ten patients were children with a median age of 2.5 (1–9) years-old and 90% received partial graft (split liver and living donor) being the hepaticojejunostomy performed in all of them. The biliary complications after LT appeared in a median time of 7 (0.2–194) months. After a median of unsuccessful balloon dilatation of 2 (1–4), biodegradable SX-ELLA biliary stents were placed due to anastomotic stenosis in 18 cases (with patent artery in 15 patients) and one case was due to non-anastomotic stenosis. Stents implantations were always feasible and no immediate major complications occurred in any case. Three adult patients presented cholangitis after 2 months of procedure and one adult patient had further endoprotesis obstruction (7 months thereafter) and hepaticojejunostomy had to be done.
Conclusions: Biodegradable biliary stents represents a new feasible option for treatment of biliary stenosis after LT.

Clinical Liver Other

BOS139 TRANSPLANT PREGNANCY REGISTRY INTERNATIONAL: PREGNANCY OUTCOMES IN LIVER TRANSPLANT RECIPIENTS WITH HEPATITIS B

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The purpose of this study is to compare pregnancy outcomes in liver recipients who were transplanted for hepatitis B with liver recipients without hepatitis B. Data were collected by the Transplant Pregnancy Registry International (TPR) via telephone interviews and review of medical records. In the TPR 10 recipients were transplanted for hepatitis B and 243 recipients were hepatitis B negative.

	Hepatitis B	No Hepatitis B	p value*
Recipients	10	243	
Pregnancies	13	462	
Pregnancy outcomes	13	477	
Drug treated hypertension during	46%	23%	NS
Graft loss within 2 years of pregnancy	23%	3%	<0.01
Live births	84.6%	71.9%	NS
Gestational age (wks)	33.1 ± 4.7	36.8 ± 3.3	<0.001
Preterm (<37 wks)	73%	38%	0.03
Birthweight (g)	2095 ± 1059	2760 ± 761	0.005

*Chi^2 or *t*-test.

Hepatitis was treated with lamivudine during 3 pregnancies; no hepatitis B antivirals were taken during the other 10 pregnancies. There were 2 rejections reported during pregnancy, one resulting in retransplant shortly after delivery and the other treated with methylprednisolone, but requiring retransplantation 4 years postpartum. Three Hepatitis B recipients (23%) lost their graft within 2 years postpartum (1 retransplant and 2 died) compared to 3% of those without hepatitis B. Adequate transplant function at last follow-up was reported in 70% of the hepatitis B recipients and 81% of the non-hepatitis B recipients. The incidence of prematurity and low birthweight infants was significantly higher in the hepatitis B pregnancies, with one neonatal death due to prematurity and one child death due to sudden infant death syndrome.
Conclusions: Pregnancy after liver transplantation generally is well-tolerated with good outcomes for mother and child. However, the small group of liver transplant recipients transplanted for hepatitis B exhibit a significantly higher risk of graft loss within 2 years of delivery and preterm low birthweight infants. Pregnancies in liver transplant recipients transplanted for hepatitis B are considered extremely high-risk and discussions prior to pregnancy should include the potential for prematurity and adverse effects on the transplanted liver.

Basic Kidney Allocation

BOS140 3-YEAR SINGLE CENTRE EXPERIENCE WITH THE "ACCELERATED ORGAN ALLOCATION SYSTEMS" (REAL, RESCUE, CENTRE OFFERS) IN THE KIDNEY TRANSPLANT PROGRAMM OF EUROTRANSPLANT

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Under pressure from the increasing reduction of organ donation in Germany, the willingness increases, to accept donor organs from the so-called "accelerated organ allocation procedures" (AOAP). These are donor organs, which have previously been repeatedly declined by other centers and are defined by extended donor criteria.

In December 2013, Recipient-Extended-Allocation (REAL) was added to the AOAP in Germany.

At our transplant center, AOAP accounts for 40% of all kidney donation offers from the Eurotransplant Kidney Allocation System (ETKAS) during the observation period from December 2013 to December 2016. Every 4th transplanted ET kidney offer comes from AOAP.

Comparing transplanted AOAP offers to transplanted ET primary offers:

- AOAP donors are significantly older and significantly more likely diabetics.
- AOAP recipients are also significantly older.
- AOAP transplants show significantly more frequently delayed graft function (> 1 dialysis post transplantation).
- AOAP transplants show a significantly worse function in the 1st year.

- AOAP recipients do not experience a significantly prolonged hospital stay.
- AOAP graft survival and patient survival did not differ significantly during the observation period.

Our retrospective analysis shows, that it is worthwhile taking part in AOAP and the general recipient risk is acceptable. Our retrospective analysis calls for a multi-center retrospective analysis on whether our results can be confirmed in general and also in long-term monitoring. Our retrospective analysis leaves open the reasons of a manifestly high refusal of ET primary offers, in view of a continuously descending of organ donation in Germany.

Clinical Kidney Donation and donor types

BOS141 EFFECT OF DONOR-RECIPIENT AGE MATCH IN EXPANDED CRITERIA DECEASED DONOR KIDNEY TRANSPLANTATION

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Purpose: Our objective was to investigate the effects of age on patient and graft survival in expanded criteria donors (ECD) renal transplantation.
Methods: Between February 2000 and December 2015, we analyzed 405 deceased donor renal transplants included 128 grafts (31.9%) from ECD. Based on the recipient age and ECD criteria classification, the recipients were divided into four groups. (Group I: Non-ECD to recipient age < 50, Group II: Non-ECD to recipient age ≥ 50, Group III: ECD to recipient age < 50, Group IV: ECD to recipient age ≥ 50 years).
Results: Among the four groups, there was significant difference in baseline characteristics (Age, BMI, cause of ESRD, Number of Kidney transplantation, the use of induction agent). The mean MDRD GFR level at 1 month, 6 months, 1 year, 3 years and 5 years after transplantation was significantly lower in patients with ECDs but MDRD GFR level at 7, 9, 10 years did not differ significantly (p = 0.183, 0.041, 0.388, respectively). There were no significant differences in graft survival (p = 0.400) and patient survival (p = 0.147).
Conclusion: Our result shows that regardless of recipient age, kidney transplants donated by expanded criteria deceased donors have similar graft and patient survival.

BOS142 DONOR BODY MASS INDEX AS A RISK FACTOR FOR DELAYED GRAFT FUNCTION

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	Hazard Ratio	95% CI	P value
Donor age ≤49 years	0.7757	0.5141–1.1707	0.2264
Donor age 50–59 years	1.0338	0.5626–1.8999	0.9147
Donor age 60–69 years	1.9526	0.8858–4.3041	0.0971
Donor age ≥70 years	2.3548	0.2204–25.1655	0.4786
Donor BMI ≤20 kg/m^2	0.4896	0.02703–8.8665	0.6289
Donor BMI 20–24.9 kg/m^2	0.6609	0.4154–1.0515	0.0804
Donor BMI 25–29.9 kg/m^2	1.2903	0.8237–2.0212	0.2657
Donor BMI 30–34.9 kg/m^2	6.0215	1.4188–25.556	0.0149
Donor BMI ≥35 kg/m^2	13.5484	1.4575–125.938	0.0220
Donor ECD	1.6935	0.9895–2.8987	0.0547
Abuse of alcohol in donor's history	1.7799	1.0679–2.964	0.0270
No induction (%)	0.8995	0.3725–2.1578	0.8126
Induction basiliximab/daclizumab (%)	1.0533	0.5202–2.1328	0.8853
Induction with ATG (%)	1.0370	0.4009–2.6823	0.9402
Tacrolimus (%)	1.6162	0.6059–4.3112	0.3375
Cyclosporine A (%)	0.6187	0.2312–1.6506	0.3375

Introduction: Delayed graft function (DGF) continues to pose a significant challenge to clinicians in the context of kidney transplantation.
Material and Methods: The objective of this retrospective, 5-year analysis is to identify the parameters of beating-heart donors and those of recipients that affect the delayed development of graft function – the necessity of dialysis treatment a week and longer after kidney transplantation.
Results: The monitored group was composed of 152 beating-heart donors and 179 recipients. DGF was identified in 32 patients (17%). The most frequent cause of DGF was acute tubular necrosis (98%). The predictor for development of DGF was the body mass index (BMI) of the donor [odds ratio 1.1473; 95% CI 1.0017–1.3140 (p = 0.0472)], and the independent risk factors were donor BMI 30–34.9 kg/m^2 [hazard ratio (HR) 6.0215; 95% CI 1.4188–25.556 (p = 0.0149)], donor BMI ≥35 kg/m^2 [HR 13.5484; 95% CI 1.4575–125.938 (p = 0.0220)], and abuse of alcohol in the donor's history [HR 1.779; 95% CI 1.0679–2.964 (p = 0.0270)] – table 1.
Conclusion: The occurrence of obesity in donors is constantly increasing, and this is related to constantly higher number of collections from donors with BMI values of more than 35 kg/m^2. In the case of accumulated risk factors for DGF (expanded criteria donor, long cold ischaemia, etc.) together with a higher BMI, it is appropriate to keep an immunologic protocol in view of possible development of DGF.

BOS143 SUCCESSFUL TRANSPLANTATION OF HUMAN KIDNEYS FROM DONOR AFTER CIRCULATORY DEATH REPUTED UNTRANSPLANTABLE BUT RESUSCITATED BY HYPOTHERMIC MACHINE PERFUSION

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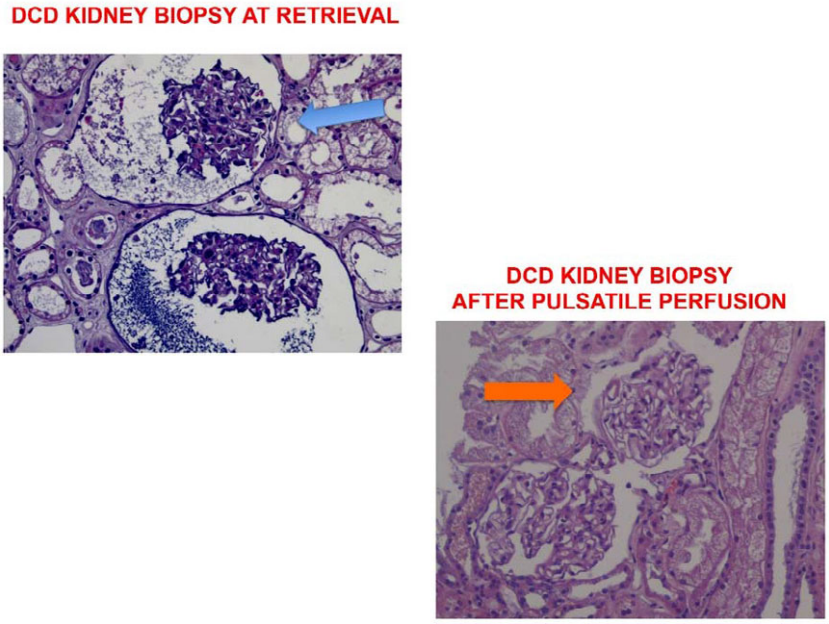
Background: Kidney donation after circulatory death (DCD) is a challenging way to face organ shortage, but 20 min warm ischemia time, imposed by the Italian law, is a risk for kidney eligibility. Macroscopic, microscopic and parameters perfusion are criteria used to give organ suitability. The most common cause of organ discard is intravascular thrombosis, however donor factors as hypotensive shock, the use of large doses of vasoactive or nephrotoxic drugs, the release of inflammatory mediators can contribute. Here, we report the successful transplantation of human kidneys that were deemed untransplantable for glomerular lesions.
Case Report: Both kidneys were procured from a 55-year-old male DCD donor who died after a cardiac arrest and treated with high dosage amines in intensive care unit for 2 days. The cold ischemic time was 24 h, the perfusion flow was 0.68 ml/min, and renal resistance was 0.33. A wedge biopsy, performed before hypothermic machine perfusion (HMP), showed widespread glomerular collapse and severe tubular necrosis but no evidence of vascular thrombi (Fig 1 upper panel). Glomerular lesions contraindicated the transplant, however we hypothesized that glomerular collapse could depend by noradrenalin vasoconstrictive effect and so we performed a second biopsy after 1 h of HMP, showing glomerular collapse disappearance (Fig 1 lower panel).
Results: The kidneys were transplanted without any complications and both had immediate urine output. Dialysis was not necessary. Hospital stay lasted 12 days. 6 months after transplantation recipients serum creatinine levels were 1.2 mg/dl (eGFR 71 ml/min/1.73 m^2) and 1.19 mg/dl (eGFR 70 ml/min/1.73 m^2), respectively.
Conclusion: In conclusion this is a singular case of reversible glomerular collapse. HMP has the potential to rescue kidneys previously deemed untransplantable because of drugs and inflammatory cytokines by improving cortical microcirculation.



BOS144

ROLE OF PRE-DONATION SERUM NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) IN ASSESSMENT OF VIABILITY OF CADAVERIC KIDNEYS FOR TRANSPLANTATION; A PILOT STUDY

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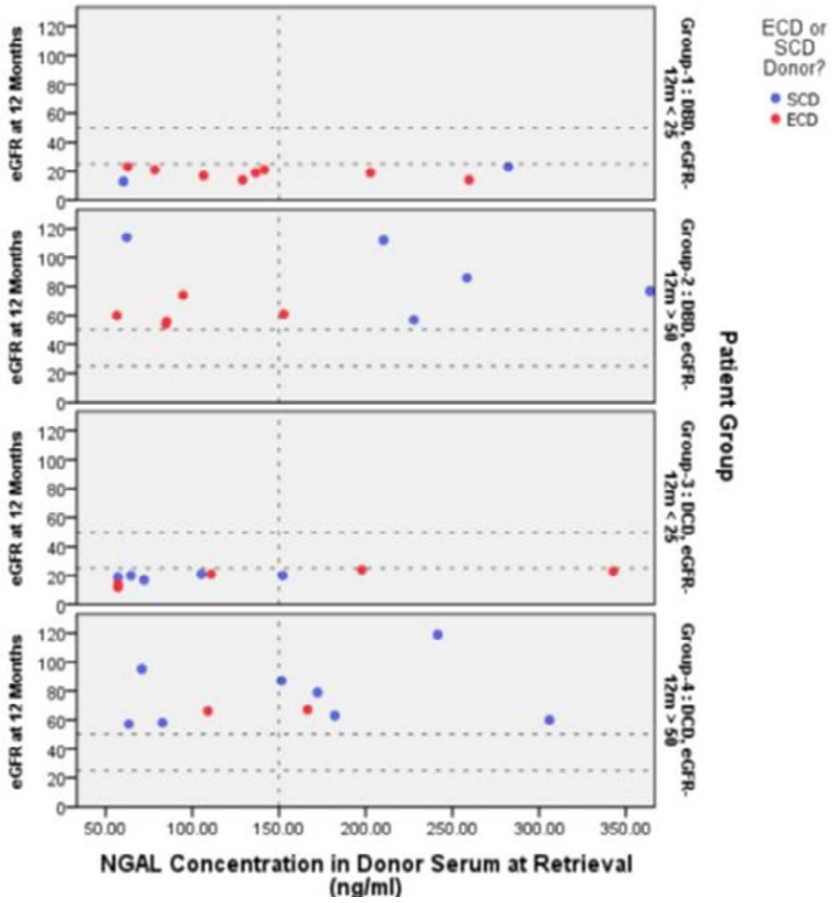
Introduction: Delayed graft function and primary non-function are unwanted outcomes in kidney transplantation, with DCD organs being affected more than DBD. There is ongoing interest in discovering biomarkers to assess kidney graft function prior to transplantation and predict outcomes. *Neutrophil Gelatinase-Associated Lipocalin* (NGAL) is a biomarker which has been shown to be sensitive in detecting acute kidney injury (AKI) with a diagnostic level being 150 ng/ml.
Methods: A retrospective study was designed to assess correlation between serum NGAL levels of DBD/DCD donors immediately prior to retrieval and post-



transplant kidney function. The source of serum samples was the QUOD tissue bank and donor samples were selected according to recipients' kidney function 12 months after transplant. In total, 20 DBD and 20 DCD samples were analysed in 4 sub-groups; half of the samples in each group had good function (GFR >50) and half had poor function (GFR <25). Serum NGAL levels were measured using an ELISA assay.
Results: Across the four sub-groups there was a 50:50 split of standard criteria (SCD) and extended criteria donors (ECD). 42.5% of all donors had an AKI diagnosed by serum NGAL levels (NGAL-AKI, serum concentration >150 ng/ml), but only 12.5% had an AKI based on serum creatinine. 66.7% of kidneys with poor 12-month function and NGAL-AKI, were from ECD donors (DBD and DCD). In contrast, only 35% of kidneys that achieved good function at 12 months were from ECDs. Only 18.2% of kidneys with good function at 12-months had NGAL-AKI.
Discussion: A high proportion of deceased donors have an NGAL confirmed AKI despite having a 'normal' pre-donation serum creatinine level. ECD donor kidneys with AKI diagnosed by serum levels are more likely to have a poor outcome at 12 months.

Group description	Group 1 DBD eGFR < 25%	Group 2 DBD eGFR > 50%	Group 3 DCD eGFR <25%	Group 4 DCD eGFR >50%
Donor age (years)	Median 54.5 Mean 57.8	Median 57 Mean 51.7	Median 58.5 Mean 56.2	Median 39.5 Mean 38.5
12 month eGFR	Median 19 Mean 18.4	Median 67.5 Mean 75.1	Median 20 Mean 19.1	Median 66.5 Mean 75.1

BOS145 OUTCOMES OF KIDNEY TRANSPLANTS FROM DONORS WITH ACUTE KIDNEY INJURY ON CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

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Body: Â Acute Kidney Injury (AKI) occurs frequently in the ICU and renal replacement therapies are often initiated in this setting. Continuous renal replacement therapy (CRRT) has become a standard in many ICU's for fluid and electrolyte management and more donors are being placed on CRRT. Once on CRRT, it is difficult to assess the true renal function of the donor, and can result high discard rates. Outcomes data from Donors with AKI on CRRT is limited.
Aim: To assess outcomes of kidney transplant recipients from donors with AKI on CRRT at the time of procurement.
Methods: Â Single Center data was collected on recipients who had received a kidney transplant from Donors with AKI on CRRT between 1/2015–10/2016. Donor demographics, donor admit Cr (DaCr), Donor Peak Cr (DpCr), and Donor Terminal Cr (DtCr), post transplant recipient Cr (Cr) at 1, 3, 6, and 12 month intervals, along with patient and graft survival were collected. All donor kidneys were biopsied and results were used in the clinical decision making for accepting kidneys.
Results: 25 recipients were transplanted from donors with AKI on a RRT. 7 donors on intermittent HD were not included in this analysis. 18 kidneys from 11 donors were transplanted from donors with AKI on CRRT. The mean DaCr was 1.56 mg/dl (0.6–2.28 mg/dl), mean DpCr was 6.67 mg/dl (1.8–9.2 mg/dl) and mean DtCr was 3.27 mg/dl (1.5–5.19 mg/dl). Mean donor age and KDPI was 27.77 years (15–52 years) and 37% (16–88%) respectively. Race: 4 AA, 3 Caucasian, 3 Hispanic, 1 Other. Post kidney transplant, mean Cr was 1.61 mg/dl (0.8–4.6 mg/dl) at 1 month, 1.02 mg/dl (0.7–1.7 mg/dl) at 3 months, 1.14 mg/dl (0.8–1.8 mg/dl) at 6 months, and 1.13 mg/dl (0.8–1.5 mg/dl) at 12 months. There was 1 death with functioning graft (Cr 1.19 mg/dl), related to a fungal infection.
Conclusions : The renal function of donors on CRRT may be difficult to interpret and may result in a high discard rate. Our single center study of kidney transplant recipients from donors with AKI had excellent outcomes. Long term prospective data is being collected.

Clinical Kidney Allocation

BOS146 WAITING LIST REGISTRATION FOR KIDNEY TRANSPLANTATION MUST IMPROVE

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Background: To investigate how the composition of the waiting list for postmortem kidney transplant has developed, and whether the waiting list reflects actual demand, we performed retrospective research and a cohort study.
Methods/Materials: We used data from the period 2000–2014 from the Dutch Transplant Foundation, RENINE and Eurotransplant Foundation. This concerned data on postmortem kidney donation, live kidney donation, the waiting list and kidney transplantation in the Netherlands.
Results: The postmortem kidney transplant waiting list included transplantable (T) and non-transplantable (NT) patients. The number of T patients declined from 1271 in 2000 to 650 in 2014, and the median waiting time between the start of dialysis and postmortem kidney transplant increased in the first period and then decreased from 4.1 years in 2006 to 3.1 years in 2014. The total number of T and NT waitlisted patients, however, increased from 2263 on 31-12-2000 to 2560 on 31-12-2014 and in the same period the number of new patient registrations increased from 772 to 1212 per year. In 31-12-2014 the reason for the NT status was not registered for 67% of all patients on a NT status for more than 2 years. A cohort analysis showed that NT-patients have a 2-times lower chance of a postmortem kidney transplant and a 2-times higher chance of leaving the waiting list without transplantation or of live donor transplantation ($p < 0.001$). This was not confounded by patient age, blood group and registration time.
Conclusion: The demand for donor kidneys remains high. The increased number of transplants resulted in a declining waiting list for T-patients while the total waiting list is getting longer. There is a difference between T and NT patients. Reasons for NT registration however are not well recorded. Waiting list registration and maintenance need to be improved, to give better insight into the real demand.

Clinical Kidney Donation and donor types

BOS147 ECMO PRIOR TO DEATH DCD DONATION, ARE TIMES MATURE TO INCLUDE THOSE DONORS IN A NEW DEDICATED CATEGORY?

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Background: The Maastricht classification has been used worldwide to describe and characterize different categories of donors after cardiocirculatory death DCD in a simple and useful manner. Extracorporeal membranous oxygenation (ECMO) has become an increasingly common mean of support for patients with salvageable cardiac or respiratory failure. ECMO prior to death (EPD) donors cannot be ascribed to any of those categories despite it is a rapidly expanding pool of donors.
Methods: A total body cardiopulmonary by-pass is performed in asystolic patients to allow brain perfusion while attempting to restore cardiac activity. Despite ECMO outcomes continue to improve a significant amount of those patients fail due to unrecoverable heart or lung failure or to a neurologic event. If they meet donation criteria and family consent is obtained, they can be considered donors after cardiocirculatory death regardless of the criteria used to certify death but they do not belong to any specific Maastricht category because the total body extracorporeal circulation is performed to save patient life and it is maintained after death certification.
Results: Since the DCD program started in Italy we were able to perform 10 kidney transplants from DCD EPD donors with good results. Mean age of the donor was 52.1 + 9.25 years, recipient mean age was 49 + 8.9 years; As far as perfusion parameters are concerned mean resistance was 0.25, mean flow was 95.12 ml/min. In 7 donors death was ascertained by neurological criteria while in 3 with cardiac criteria. Mean follow up was 2.75 years (min 0.19 year, max 7.56 years). We experienced 1 case of Primary Non function (PNI), 60% of Delayed Graft Function (DGF), 0% acute rejection.
Conclusions: Organ coming from EPD donors are well preserved even after several hours of ECMO and since and previsions show that more donors belonging to this category will be recruited in the next few years they deserve to be included in a new dedicated category.

BOS148 CONTROLLED DONATION AFTER CIRCULATORY DEATH (CDCD) DONORS: AN OPTIMAL DONOR!

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Since 2014 in France, we started a cDCD program characterized by the introduction of normothermia regional perfusion (nRP) and selection criteria as donor age ≤65 years, functional warm ischemia time (fWIT) <30 min (liver), <90 min (lung), <120 min (kidney), and short cold ischemia times (CIT).

Potential recipients were recipients awaiting a 1st transplant.

Out of 119 potential cDCD donors (2015/2016), 62 have been retrieved, mean age 49 years. Causes of death are mainly hypoxic brain damage (59%) and trauma/head injury (27%). Mean fWIT are 36 min (kidney only), 22 min (liver and kidney). nRP was used in all utilized donors, the mean circulatory arrest delay was 25 min. Average renal CIT was 10.4 h. Mean fWIT are 36 min (kidney only), 22 min (liver and kidney). Average renal CIT was 10.4h.

The aim of this study was to compare primary non function (PNF), delayed graft function (DGF) and length of stay in hospital after 1st single kidney transplantation (KTR) with 2 types of donors: cDCD (113 KTR from 12/2014 to 12/2016) and matching donors after brain death (DBD) aged 18–65 years (1050 KTR from 1/2013 to 12/2015). Rate of PNF (2 vs. 3%), and mean renal clearance (49 vs. 44 ml/min) at discharge are similar. DGF rate (9% vs. 18%) and dialysis number in case of DGF are significantly lower in case of cDCD.

28 liver transplants and 3 bilateral lung transplant were also performed without EAD and with excellent transplant outcomes.

These good results ensue from a consensual national protocol, which aims were to limit warm ischemia times and injuries, thanks to the use of nRP, optimal graft preservation and recipient selection. cDCD donors might represent a source of kidneys giving results equivalent to SCD donors!

BOS149 IS THERE A LIMIT TO THE USE OF VERY EXTENDED CRITERIA DONORS IN KIDNEY TRANSPLANTATION?

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The use of very extended criteria donors has increased in the last years related to the paucity of donors and the increasing age of recipients. However, doubts about their viability make extremely difficult the decision about their allocation.
Objective: To analyze evolution of kidney transplants performed with kidneys from donors older than 80 years.
Material/Methods: We compared, in a retrospective study, kidney transplants from donors older than 80 years (D ≥ 80) vs. donors younger than 80 years (D < 80). From January 2012 to December 2016, 258 kidney transplants were performed, 65% (176) of them with expanded criteria donors, with a mean follow-up of 24.46 ± 18.24 (0–60.9) months.
Results: Nineteen kidney transplants were performed with kidney from D ≥ 80, and 157 with D < 80. Median recipient age in D ≥ 80 group was 68.5 ± 9.8 years vs. 60.6 ± 9.8 years in the group of D < 80 ($p < 0.001$). No differences were found about recipient gender between groups. Mean donor age in D ≥ 80 was 81.8 ± 1 years vs 67.5 ± 6 years in D < 80 ($p < 0.001$). In D ≥ 80 group, there was a greater proportion of female donors (77.8% vs 50%, $p = 0.02$). No differences were found in blood pressure ($p = 0.636$) or cerebrovascular death ($p = 0.663$). Delayed graft function was more frequent in D ≥ 80 ($p = 0.06$) in spite of a shorter cold ischemia time (14.5 ± 6.1 vs. 17.8 ± 5.1 h, $p = 0.022$). Early acute rejection episodes were similar in both groups. Renal function was significantly lower in D ≥ 80 during the follow-up. Graft survival was lower in D ≥ 80 ($p = 0.041$) without differences in patient survival. There have been four graft losses in the early postoperative period in D ≥ 80 group (two graft thrombosis and two primary non-function).
Conclusions: Kidneys from D ≥ 80 have allowed transplant access to older recipients. The high rate of early graft losses reflects a greater vascular risk and a lower capacity to recovery of ischemia-reperfusion injuries, making essential the continuous review of results.

BOS150 A BRIDGE TOO FAR? OUTCOMES OF EXPANDED CRITERIA KIDNEY TRANSPLANTATION

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Background: The critical shortage of suitable organ donors has led to increased use of Expanded Criteria Donor (ECD) kidneys, with poorer reported outcomes. We aim to compare outcomes with standard criteria donors (SCD) and investigate donor and recipient variables associated with graft failure and mortality.
Methods: A retrospective analysis of all adult kidney transplants carried out over a 36-month period at a single centre was performed. Graft and recipient outcome data were collated along with recipient, donor and transplant factors. Graft failure was defined as a return to end-stage renal failure (eGFR <15 ml/min).
Results: 708 kidney transplants were performed with a mean recipient age of 52 years (18–80), with 40% ECD kidneys. The average waiting time was 864 days (2–7032). Delayed graft function (DGF) was reported in 26% of cases, with primary non-function in 3.4%. Recipients with DGF had longer total ischemia time (819 vs. 575 min, $p < 0.0001$). Total mortality was 3.5%. 2.1% of recipients experienced graft failure. ECD kidney recipients were older (58 vs. 48 years, $p < 0.0001$) and had higher rates of DGF (58% vs. 22.6%, $p < 0.0001$). Survival was reduced in ECD recipients (log-rank, $p = 0.026$) and diabetic recipients (log-rank, $p = 0.003$). Diabetic recipients receiving an ECD kidney had further reduced survival ($p = 0.021$). Within the SCD group, diabetes was not associated with reduced survival ($p = 0.152$). In a multivariate Cox regression model, recipient diabetes history conferred a 3.6-fold increased risk of graft failure. In the Cox mortality model, recipient diabetes and DGF were the only significant hazards (HR 3.124 and 3.693, $p < 0.05$).
Discussion: ECD kidney recipients experience a higher rate of DGF, graft failure and mortality than SCD recipients. Moreover, DGF and recipient history of diabetes are significant predictors of mortality. Therefore, the combination of ECD kidneys and diabetic recipients should be minimized to decrease the risks of graft failure and mortality

Basic Kidney Allocation

BOS151 COMPARING THE EURO TRANSPLANT KIDNEY ALLOCATION SYSTEM WITH A COLOR PRIORITY KIDNEY ALLOCATION SYSTEM

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Kidney allocation of cadaveric donors to end stage renal disease patients in a waiting list must be as equitable as possible. This equity is achieved defining allocation rules that balance utility and justice, i.e. minimizing the number of HLA mismatches between donor and recipient while trying to select those recipients with higher waiting times for a transplant. Here we compare the EuroTransplant Allocation System (ETKAS) with a proposed Color Priority Kidney Allocation System (CPKAS). The CPKAS classifies patients in the waiting list in four color groups (red, orange, yellow and green) according to patients waiting time on dialysis and cPRA level (table I). Patients with longer waiting time or cPRA >85% are classified as orange and those with lower waiting time are classified as green. Within each color group patients with a negative virtual crossmatch are ordered from the lower number of HLA mismatches with a potential cadaveric donor.

We generate data for a simulated waiting list of 500 recipients and 70 cadaveric donors and applied both ETKAS and CPKAS to obtain two groups of selected recipients for each system. Mann-Whitney Test was used to compare ages and time on dialysis of selected patients and Chi-square test was used to compare cPRA and HLA mismatches frequencies by allocation system.

Table I

Kidney allocation colour system

	Not ECD		ECD	
Recipients ≤ 65 years old	Clinically Urgent	RED	Clinically Urgent	Recipients > 65 years old
	cPRA ≥ 85% or ToD ≥ 3rd Quartile[1]	ORANGE	cPRA ≥ 85% or ToD ≥ 3rd Quartile[1]	
	cPRA ≥ 50% or ToD ≥ Median[1]	YELLOW	cPRA ≥ 50% or ToD ≥ Median[1]	
	cPRA < 50% and ToD < Median[1]	GREEN	cPRA < 50% and ToD < Median[1]	

ECD – Extended Criteria Donor; cPRA – calculated PRA; ToD – time on dialysis
[1] wait listed patients' time from first dialysis to transplantation

We don't find differences in ages between recipients selected by ETKAS and CPKAS. Median time on dialysis was higher in those patients select CPKAS than by ETKAS (67 months vs 63 months, $p = 0.04$). In patients selected by ETKAS 84% have 3 or less HLA mismatches with their potential donor while in the selected patients with CPKAS this value drops to 60% ($p < 0.01$). We don't' find statistical significant differences between cPRA frequencies in both groups.

In conclusion, when compared to ETKAS the previously proposed CPKAS selects waiting list patients with longer waiting times on dialysis but with more HLA mismatches with their donors.

Basic Kidney Donation and Donor Types

BOS152 METABOLIC DYSREGULATION AND MITOCHONDRIAL DYSFUNCTION DEFINE INJURY PROFILES OF DONOR KIDNEYS AFTER BRAIN DEATH AND ISCHAEMIA-REPERFUSION

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Background: DBD and DCD organ donors are an essential source for kidney transplantation. However, brain death and warm ischaemia affect the organs rendering them more susceptible to reperfusion injury once transplanted. Understanding how kidneys are injured by these processes will allow to develop novel strategies protecting organs in the donor, especially in higher risk donors.
Methods: In pre-clinical Brain Death (BD) and Ischaemia-Reperfusion Injury (IRI) models (unilateral 45 min renal ischaemia followed by 24 h reperfusion), cellular pathways in kidney biopsies were found to be altered compared to healthy controls using proteomics and metabolomics techniques. Omics findings were further validated (by western blot, enzymatic, amperometric and luminescent assays) and highlighted disturbances in ATP, mitochondrial function and oxidative stress.
Results: Proteomics and metabolomics results suggested extensive mitochondrial dysfunction. Mitochondria isolated from DBD and IRI kidneys both showed decreased O_2 consumption (Figure 1) ($p < 0.05$) which correlated with decreased tissue ATP levels, compared to controls. In DBD, mitochondrial morphology showed significant fragmentation and mitochondrial dysfunction was associated with increased inflammatory response (NFkB mRNA levels, $p = 0.01$) and increased oxidative stress ($p = 0.01$), when compared to controls.
Conclusion: BD and IRI result in concerted alterations of metabolic pathways in the kidney leading to dysregulated mitochondria and oxidative stress contributing to injury of the graft. This renders kidneys more susceptible to reperfusion injury once transplanted and potentially increases the risk of DGF. DBD and DCD donor samples from the UK QUOD biobank are currently being investigated to establish whether these phenotypes are also present in deceased human donors.

Mitochondrial protective strategies are now possible interventions and may reduce injury to donor organs improving outcomes after transplant.

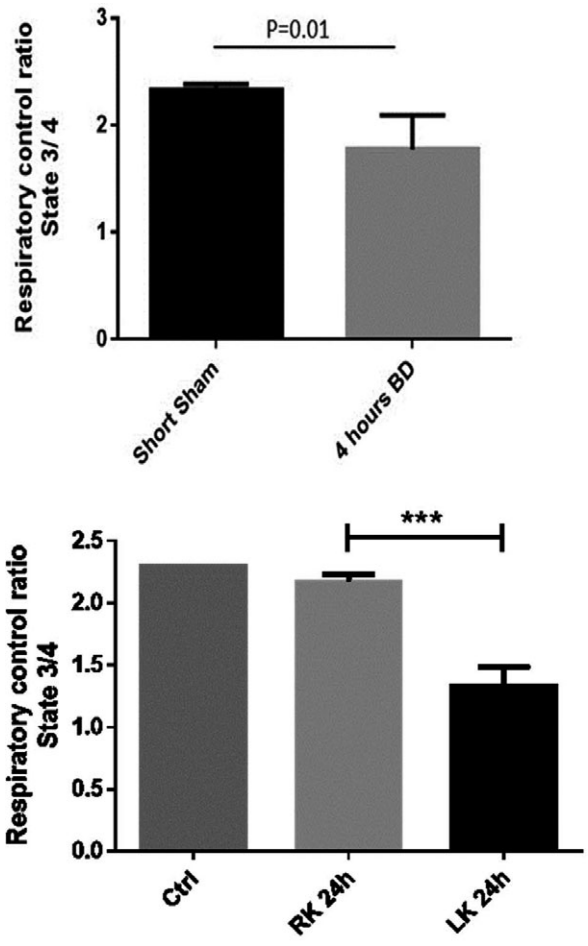

Fig. 1. O_2 consumption is significantly decreased in BD and ischaemic (LK 24h) kidneys compared to controls (short sham; RK 24h)

BOS153 MTOR-INHIBITOR RAPAMYCIN IS UNABLE TO INDUCE AUTOPHAGY AND ATTENUATE TISSUE INJURY AND APOPTOSIS IN THE LIVER AND KIDNEY OF BRAIN-DEAD RATS

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Introduction: Donor brain death (BD) increases tissue injury and apoptosis. Apoptosis is counteracted by autophagy, a protective, stress-adaptation mechanism regulated by mammalian target of rapamycin (mTOR). Autophagy disregulation has been linked to ischemia/reperfusion-injury and sepsis. Whether autophagy is affected after BD is unknown. This study investigated how BD affects autophagy in the liver and kidney of brain-dead rats. Second, effects of autophagy upregulation using mTOR-dependent rapamycin were studied.
Methods: BD was induced in mechanically ventilated rats by inflation of an epidurally-placed balloon catheter. Vehicle (EtOH) or rapamycin (1 mg/kg) was administered intraperitoneally 2 h prior. After 4 h of BD, plasma and tissue were collected and the left kidney normothermically perfused for 90 min in an isolated perfused kidney model. Tissue injury and function were assessed with routine biochemistry. Autophagy (p62, Beclin 1, LC3I/II), apoptosis (Bax, Bcl2, ratio, cC3), and mTOR activity (phospho-S6) markers were analysed with Western blot and qPCR.
Results: Brain-dead animals had reduced renal levels of autophagic marker LC3-II, associated with increased activation of autophagy-inhibitor mTOR (pS6/S6), which correlated to increased autophagy degradation substrate p62 and cC3. In the liver, mTOR activation was seen without changes in LC3-II, p62, or cC3. Autophagy upregulation with rapamycin did not attenuate BD-induced

injury (ALT, AST, creatinine, urea, LDH) or apoptosis (Bax, Bcl2), induce autophagy (Beclin 1, LC3, p62), or improve renal function after reperfusion.
Conclusion: BD upregulated autophagy-inhibitor mTOR and reducing autophagy in the kidney but not liver. Inhibition of mTOR with rapamycin did not induce autophagy or attenuate injury or apoptosis in the liver or kidney, nor improve renal function after reperfusion. Thus, rapamycin did not improve BD-induced injury and suggests autophagy is regulated via an mTOR-independent pathway during BD.

Basic Liver Ischemia-Reperfusion and Preservation

BOS154 GLYCOGEN SYNTHASE KINASE 3 BETA (GSK3B) AND VOLTAGE-DEPENDENT ANION-SELECTIVE CHANNEL 1 (VDAC1) INHIBITION IN ORTHOTOPIC LIVER TRANSPLANTATION USING IGL-1 PRESERVATION SOLUTION

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Background: The relevance of mitochondrial GSK3beta and VDAC 1 in liver transplantation has not fully investigated. In this communication we explored the involvement of Glycogen Synthase Kinase-3β (GSK3β) and Voltage-Dependent Anion Channel (VDAC) in the mitochondrial protection after transplantation when IGL-1 solution was used and compared to UW.
Methods: Preservation of the livers was performed for 8 hours under different UW, IGL-1 and IGL-1 supplemented with trimetazidine (TMZ) at 10 μM (IGL-1 + TMZ) vs UW. Sprague-Dawley rats were subjected to orthotopic liver transplantation and sacrificed at 24-h reperfusion. Samples were collected (blood and tissue) for the subsequent analyses. We analyzed transaminases (AST/ALT), HMGB protein levels, Glutamate dehydrogenase (GLDH) and oxidative stress. By western blot was analyzed AKT and their direct substrate, GSK3-β and VDAC; as well as apoptotic markers (caspase 3, 9, and cytochrome c). Endoplasmic Reticulum Stress (as GRP78, pPERK, ATF4 and CHOP alterations) was also evaluated. Histological findings were also performed.
Results: IGL-1 + TMZ solution reduced both liver (AST/ALT) and mitochondrial damage (GLDH) while decreasing oxidative stress (MDA) too when compared with the other solutions. This resulted in the phosphorylation of AKT and, as a consequence, its direct substrate: the GSK3-β. This protection is related with a decrease in ER stress markers (GRP78, p-PERK, ATF4 and CHOP) and a decrease of the phosphorylated VDAC. In IGL-1 + TMZ solution, caspases 3, 9 and cytochrome C protein levels were also reduced when compared to the rest of the groups UW and IGL-1 alone. Amelioration of liver graft structure was also confirmed by the histological findings.
Conclusion: IGL-1 preservation solution increases liver protection against I/R injury through the decrease of ERS and cell death prevention due to the inhibition of GSK3β and VDAC.

BOS155 HIGHLIGHTS OF PROTECTION MECHANISMS INVOLVED IN LIVER GRAFT COLD ISCHEMIA PRESERVATION: A COMPARISON BETWEEN IGL-1 AND HTK SOLUTIONS

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Background: IGL-1 is a good alternative to UW (standard goal), but comparative investigations with another commercial solutions, such as HTK, used in liver transplantation are poor. In this communication, we evaluate the cold ischemia injury and the differential preservation mechanisms when fatty liver grafts (60–50% steatosis) were preserved in IGL-1 and HTK solutions for 24hC at 4°C respectively.
Methods: Male Zucker Obese rats (10 weeks) were classified as follows: *Group 1 (IGL1)*= liver grafts washed with 50 mL of IGL-1 and preserved 24 h at 4°C with IGL-1. After 24 h livers were rinsed with 20 mL of Ringer-Lactate (RLS). *Group 2 (HTK)*= Same as Group 1 but using 125 mL of HTK and preserved 24 h at 4°C. *Group Control*: liver grafts were flushed via portal vein with RLS immediately after laparotomy without cold storage. We evaluated liver injury (AST/ALT) and mitochondrial damage (glutamate dehydrogenase, GLDH); as well as cytoprotective factors such as AMPK and p-AMPK, eNOS and p-eNOS which well correlated with the concomitant alterations in liver reticulum stress (ERS) markers (GRP78, PERK) and autophagy markers (Beclin 1 and LCBIII), respectively.
Results: AST and ALT levels showed a better protection of fatty liver grafts preserved in IGL-1 when compared to HTK. This was consistent with a better mitochondrial protection (lower GLDH levels) during cold storage which was accompanied by enhanced increases in AMPK and e-NOS expression of preserved liver grafts in IGL-1 vs HTK. ERS changes were also prevented in IGL-1 solution, as revealed by GRP78 and PERK decreased levels. Autophagy changes (Beclin-1 and ATF4) were accompanied by increases and liver apoptosis prevention during IGL-1 cold storage vs HTK.
Conclusion: IGL-1 protects better the liver graft than HTK. This is due to the enhanced activation of e-NOS, AMPK expressions and the prevention ERS, which in turn lead to the prevention of liver apoptosis.

BOS156 A NEW PREDICTING TOOL FOR EXPERIMENTAL LIVER TRANSPLANTATION – LIVE TISSUE STAINING

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The ischemia reperfusion injury is a main contributor to early graft dysfunction, which leads to costly and lengthy follow-up treatments or even organ loss in clinical liver transplantation. To address the ever-increasing gap between patients on waiting list and organs available for transplantations, more and more marginal grafts are transplanted.
Methods: To monitor graft quality prior to transplantation are therefore highly desirable to optimize clinical outcome.

In an experimental model we used life confocal microscopy to assess murine liver graft quality. Six to ten-week-old male animals were subjected to a methionine-choline-deficient (MCD) diet causing non-alcoholic fatty liver disease (NAFLD), or to the Lieber DeCarli diet producing alcohol-induced liver injury. Untreated animals served as control. In each group liver biopsies were analyzed after 45 minutes' warm ischemia time (WIT) induced by liver pedicle occlusion, 24 hours' cold ischemia time (CIT) respectively. All clamped livers were reperfused for 4 h. Graft quality assessment was performed by measurement of serum transaminases, standard histopathology, assessment of cytokine expression profiles, assessment of oxidative stress and live confocal microcopy.

After CIT and WIT liver grafts showed a decrease in cell viability when compared to naïve animals ($p < 0.05$) as assessed using life confocal microscopy. Animals exposed to the MCD diet showed significantly lower cell viability within the liver biopsies after CIT as well as after WIT when compared to control animals ($p < 0.05$). Similar results were obtained from the analysis of cell viability of animals fed with the LDC diet. Results from confocal microscopy were then correlated with the results from detection of serum transaminases of, standard H&E staining the expression of proinflammatory cytokines as well as markers for oxidative stress.

Our data demonstrate that confocal microscopy is well suitable to detected organ damage prior to transplantation.

Clinical Liver Ischemia-Reperfusion and Preservation

BOS157 IMPACT OF DECEASED BRAIN DONORS CHARACTERISTICS ON LIVER PERFUSATE LYMPHOCYTE SUBSETS: SINGLE CENTER ANALYSIS

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Background: Interstitial liver T-lymphocytes, natural killer (NK) T cells and NK cells play important roles in both innate and adaptive immunity and liver ischemia/reperfusion injury (IRI) regulation.
Methods/Materials: Phenotypes and concentrations of lymphocyte subsets were analyzed retrospectively in a consecutive series of whole liver graft perfusates (LPs), and matched with 49 adult liver donor after brain death (DBD) characteristics. Density gradient centrifugation was used to purify the liver infiltrating cells from LPs, obtained during the back-table surgical time. Lymphocytes phenotype and relative percentages were assessed by flow cytometry after staining with anti CD3, CD4, CD8 and CD56 antibodies. NK cell activation phenotype was assessed by staining with NKp30, NKp44, NKp46 and NKG2D antibodies.
Results: Percent T-cell number was significantly associated with cold ischemia time ($p = 0.02$), and Early-Graft-Loss/Donor Risk-Index (EGL-DRI) score ($p = 0.01$). Increasing the percentage of T-cell by one the EGL-DRI decreases by 0.06 (p-value = 0.006). LP NK content was strongly associated with donor age and body mass index ($p = 0.003$ and $p = 0.02$, respectively).

Conclusions: Our study indicates novel potential biomarker to target hypoxic injury and may provide relevant mechanistic insights into the pathogenesis behind IRI.

Translational Liver Ischemia-Reperfusion and Preservation

BOS158 DEVELOPING A NON-INVASIVE SPECTROSCOPIC TECHNIQUE FOR ASSESSING THE BIOMOLECULAR EFFECTS OF NORMOTHERMIC REGIONAL PERFUSION

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Background: Normothermic regional perfusion (NRP) re-establishes *in situ* circulation to the abdominal organs. Clinical evidence suggests that it substantially decreases the risk of injury to the liver that would otherwise occur under ischemia. Despite the increased use of the technique in the organ retrieval window, there remains an unmet need for real time assessment of NRP-treated livers prior to transplantation.

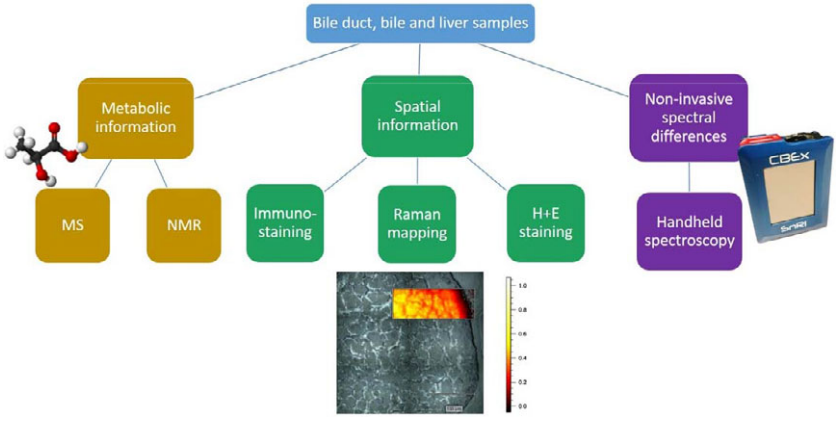
Here, we present preliminary work towards a non-invasive, label-free method for assessing the biomolecular effects of normothermic regional perfusion.

Method: The baseline ischemic injury was determined using a two-hour warm ischemia ($n = 1$). A porcine model of donation after circulatory death (DCD) with 45 minutes of warm ischemia and 2 hours of NRP was developed. *In situ* spectral data from six pigs was obtained prior to cardiac arrest (CA), at the end of warm ischemia and at the end of NRP using a 785 nm handheld Raman spectrometer. A minimum of two readings were obtained from the right lobe and quadrate lobe in all pigs. Liver and bile duct biopsies before CA and after warm ischemia and NRP were collected for analysis using nuclear magnetic resonance spectroscopy (NMR), immunostaining and Raman microspectroscopy.

Results: NMR coupled with Raman spectroscopy shows that liver and bile duct samples exhibit morphological and biomolecular variations pre-CA, during ischemia and during NRP. Moreover, spectral readings taken in real time using handheld Raman demonstrate the ability of non-invasive spectroscopy to detect changes in the liver during NRP.

Conclusion: Raman spectroscopy could be used as a bedside tool to assess the efficacy of NRP and determine the recovery of the liver graft prior to transplantation.

Figure 1. Schematic diagram showing the various types of techniques that have been applied to samples of liver, bile duct and bile obtained from a porcine model of donation after circulatory death.



Basic Liver Ischemia-Reperfusion and Preservation

BOS159 HYPEROXIC NORMOTHERMIC PERFUSION IS ASSOCIATED WITH HIGH LEVELS OF SYNDECAN-1 AND PROTEIN CARBONYL SUGGESTING PRODUCTION OF REACTIVE OXYGEN SPECIES

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Background: Normothermic ex situ liver perfusion (NESLiP) was developed to facilitate assessment of marginal livers and minimize cold ischaemia. Following initial experience with 6 NESLiP liver transplants, where 5 patients suffered post reperfusion syndrome and/or profound vasoplegia, we sought to investigate if this could be related to reactive oxygen species (ROS) formation due to the use of high perfusate oxygen tensions.

Methods: We compared 5 livers undergoing NESLiP at high and 5 at low oxygen tensions, measuring perfusate concentrations of syndecan-1 and liver tissue protein carbonyls from samples taken 3 to 4 hours after the onset of perfusion.

Results: Hyperoxic livers had higher levels of protein carbonyls ($p = 0.04$) and higher perfusate concentrations of syndecan compared to livers perfused at lower oxygen tensions (see table). Median hyperoxia perfusate pO_2 was 75 kPa, normoxic pO_2 was 20 kPa.

Conclusion: High oxygen tensions have previously been shown to cause reperfusion injury and refractory vasoplegia from generation of ROS and reactive nitrogen species in animal models and in cardiac patients undergoing cardiopulmonary bypass. NESLiP in the presence of high oxygen tensions appears to be associated with ROS production (higher carbonyls) with associated glycocalyx damage (higher syndecan). Subsequent clinical perfusions ($n = 10$) using air in place of oxygen to oxygenate the perfusate have been associated with neither post reperfusion syndrome nor vasoplegia.

Translational Liver Ischemia-Reperfusion and Preservation

BOS160 AN OXYGENATED AND TRANSPORTABLE MACHINE PERFUSION SYSTEM FULLY RESCUES LIVER GRAFTS EXPOSED TO LETHAL ISCHEMIC DAMAGE IN A PIG MODEL OF DCD LIVER TRANSPLANTATION

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Background: Control of warm ischemia (WI) lesions that occur with donation after circulatory death (DCD) would significantly increase the donor pool for liver transplantation. We aimed to determine whether a novel, transportable, oxygenated and hypothermic machine perfusion device (HMP Airdrive® system) improves the quality of livers derived from DCDs using a large animal model.
Methods: Cardiac arrest was induced in female large white pigs by IV injection of potassium chloride. After 60 min of WI, livers were flushed in situ with HTK and subsequently preserved either by simple cold storage (WI-SCS group) or HMP (WI-HMP group) using Belzer-MPSTM solution. Liver grafts procured from heart-beating donors and preserved by SCS served as controls. After 4 hr of preservation, all livers were transplanted.
Results: All recipients in WI-SCS group experienced primary non-function and died within 6 hours after transplantation. In contrast, the HMP device fully protected the liver against lethal ischemia/reperfusion injury, allowing 100% survival rate. A post-reperfusion syndrome was observed in all animals of the WI-SCS group but none of the control or WI-HMP groups. These phenomena caused a significant increase in fluid challenge and catecholamine needs in WI-SCS group. After reperfusion, HMP-preserved livers functioned better, and showed less hepatocellular and endothelial cell injury, in agreement with better-preserved liver histology relative to WI-SCS group. In addition to improved energy metabolism, this protective effect was associated with an attenuation of inflammatory response, oxidative load, endoplasmic reticulum stress, mitochondrial damage and apoptosis.
Conclusions: This study demonstrates for the first time the efficacy of the transportable HMP Airdrive® device to protect liver grafts from lethal ischemic damage prior to transplantation in a clinically relevant DCD model.

BOS161 SPLIT LIVER EX-SITU OXYGENATED MACHINE PERFUSION: A NOVEL APPROACH TO ORGAN PRESERVATION AND TREATMENT

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Background: *Ex-situ* machine perfusion (MP) is a promising method to improve organ viability for transplantation and is being used in various clinical trials. However, the heterogeneity of clinical deceased donor livers makes it difficult to compare the results of MP to static cold storage (SCS), both in clinical and pre-clinical research. We therefore developed a split liver *ex-situ* MP technique to provide matched controls for each liver.
Methods: We adapted our previously designed subnormothermic (21°C) MP protocol for whole liver grafts, to test whether two lobes of the same liver would be comparable to each other and to a whole graft during perfusion. Eleven discarded human livers with research consent were included. Livers were split anatomically into right and left lobes. Each lobe was perfused separately for 3 hours. Hemodynamics and biochemical profile of each lobe were monitored at regular time intervals.
Results: As with whole liver perfusions, each lobe exhibited decreasing venous and arterial resistance and lactate levels, which were not significantly different between the right and left lobe within each liver. Overall bile and ATP production was low in the split livers compared to whole liver perfusions. Liver ALT release was slightly higher in left lobes compared to right lobes but didn't reach statistical significance.
Conclusion: Single liver lobes behave similarly to whole livers during MP, and to each other. Split liver perfusion is a novel approach that may allow direct comparison of different preservation techniques and treatments on the same liver, circumventing the need for extremely large numbers of experimental and control livers necessary with the wide variability of discarded human livers. Optimizing perfusion techniques using this system may eventually increase the supply of viable donor organs so that fewer need to be discarded.

Figure-1: Behavior of single liver lobes during MP shown by resistance (A), ALT (B) and Lactate release (C).

Basic Liver Ischemia-Reperfusion and Preservation

BOS162 HMGB1 IS MOST EFFECTIVE THAN ACETYLCHOLINE TO PROTECT STEATOTIC LIVER TRANSPLANTATION FROM CADAVERIC DONORS

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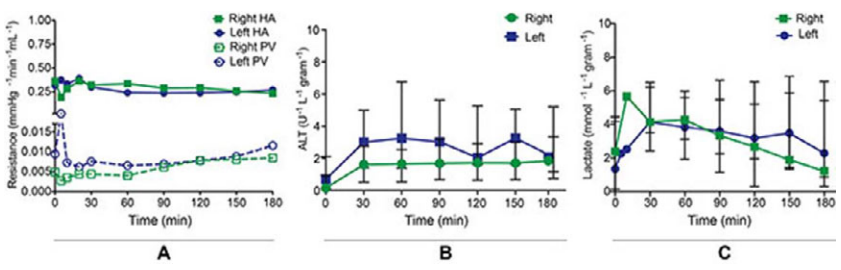
Background: High percent the liver grafts undergoing transplantation derive from brain dead (BD) donors, which may also show hepatic steatosis, being both characteristics risk factors in liver transplantation. Nevertheless, BD reduces the tolerance of liver grafts to the preservation/reperfusion injury. Ischemic preconditioning (IP) shows benefits when applied in liver from non-BD patients like hepatectomies, whereas it has been less promising in BD clinical situations. This study evaluated how the activation of cholinergic pathway and HMGB1 treatment only or in combination with IP affects steatotic liver grafts undergoing transplantation.
Methods: Steatotic liver grafts from non-BD and BD-donors were cold stored for 6 h and then transplanted. After 4 h of reperfusion, hepatic damage was analyzed. Four strategies, acetylcholine and HMGB1 pre-treatments only or in combination with IP was induced. The effects on hepatic damage and their underlying mechanisms were characterized.
Results: The presence of BD exacerbated hepatic damage and reduces HMGB1 expression. Acetylcholine treatment reduced hepatic damage after transplantation in BD donors, through PKC, increased antioxidants and reduced lipid peroxidation, nitrotyrosines and neutrophil accumulation. HMGB1 treatment increases the PI3K/Akt pathway and this result in protection against neutrophil accumulation, oxidative stress, and hepatic damage. On the other hand, the combination of acetylcholine and IP conferred protection but combination of HMGB1 and IP shows additional benefits and stronger protection than acetylcholine treatment or HMGB1 alone. These superior beneficial effects



may derive from the anti-oxidant and anti-inflammatory properties of different mediators generated by IP which may act dependently of HMGB1.
Conclusions: We herein propose that combination of HMGB1 and IP or acetylcholine and IP as feasible and protective strategies to reduce the adverse effects of BD and improve the quality of liver grafts.

Clinical Liver Ischemia-Reperfusion and Preservation

BOS163 IMPACT OF PRESERVATION SOLUTION ON EARLY ALLOGRAFT DYSFUNCTION (EAD) AND GRAFT SURVIVAL AFTER LIVER TRANSPLANTATION USING EXPANDED-CRITERIA-DONORS (ECD)

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Background: Optimization of donor management and organ preservation offers the most realistic w ay to improve both the quality and the pool of current organ supply.
Aim: Comparing the early liver function and the long-term graft survival of ECD transplanted grafts that have been stored either in Celsior (CEL), Histidine-Tryptophan-Ketoglutarate (HTK), Institut Georges Lopez (IGL-1), *Solution de Conservation des Organes et des Tissus* (SCOT) or University of Wisconsin (UW).
Methods: From 2007 to June 2015, 803 out of 1085 (74%) LTs were performed in a single center using ECD grafts preserved with IGL-1 ($n = 293$), CEL ($n = 220$), UW ($n = 206$), SCOT ($n = 33$) or HTK ($n = 26$). The solution was chosen according to the preference of the local procurement team. Kinetics of liver function, EAD, vascular, biliary complications, and graft survival were compared for the 5 groups. Were considered as ECD, donors with: age>55 yrs or BMI>27 kg/m2 or cold ischemia time >14 hours or macrovesicular steatosis >60%. The EAD was defined by the method of Olthoff.
Results: The incidence rate of EAD was higher with SCOT (56%) and HTK (46%) compared to UW (38%), CEL (38%) and IGL-1 (35%) ($p < 0.05$) (Table 1). These results are in concordance with higher peaks of SGOT, SGPT and INR ($p < 0.01$), and with a higher rate of vascular and biliary complications with these two solutions. However, serum bilirubin at day 1 was the far highest only in SCOT ($p < 0.05$). The graft survival at 1 year was similar with SCOT (82%), HTK (83%), CEL (85%), UW (85%) and IGL-1 (89%).
Conclusion: CEL, UW and IGL-1 give better results than SCOT and HTK in terms of early graft function after cold static preservation of ECD liver grafts. However these better results did not impact graft survival.

BOS164 POSTREPERFUSION SYNDROME IN LIVER TRANSPLANTATION: WHAT IS THE IMPACT ON SHORT-TERM SURVIVAL?

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Introduction: Postreperfusion syndrome (PRS) is a state of systemic hemodynamic instability, following graft reperfusion and considered as a poor prognosis factor after liver transplantation (LT).
Objective: To evaluate the impact of PRS on postoperative outcome after LT.
Methods: From September 2013 to April 2016, all consecutive LT performed at our center were retrospectively analyzed. PRS was defined as a decrease of mean arterial pressure greater than 30% below the baseline during more than 1 min during first 5 minutes following graft reperfusion. Postoperative complications, the graft survival and overall survival were analyzed.
Results: During this period, 145 LT were performed. Median age was 54 years (18–68). PRS occured in 30% of cases ($n = 41$), Population with or without PRS were comparable. PRS was associated with an increase of 90-day mortality (15% vs 4%, $p = 0.016$), major complications (Dindo-Clavien >3) (58% vs 35% = 0.008), and graft loss at 6 months (27% vs 6%, $p = 0.001$). In the PRS group, there was more postoperative renal failure (30% vs 56%, $p = 0.033$) and more primary graft dysfunction (10% vs 1%, $p = 0.008$). Cold ischemia duration was no statistical significance between group with or without PRS. In multivariate analysis, PRS (OR = 5.4 IC95 (1.7–17), $p = 0.004$) and transfusion (OR = 1.2 CI: 95 (1.1–1.6), $p = 0.004$) were independent factor of graft loss at 6 months.
Conclusion: PRS is an independent risk factor for major complications and graft loss at 6 months.

BOS164.1 THE EDINBURGH LIVER FUNCTION (ELF) SCORE RAPIDLY DEMONSTRATES SIGNIFICANT GRAFT ENHANCEMENT IN STUDIES OF LIVER OPTIMISATION

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Background: Graft optimisation is a major initiative in liver transplantation. However, functional assessment after intervention remains a serious challenge, as currently available end points, such as non-function, death, re-transplantation, or other binary outcome scores, are too infrequent or too coarse.
Aim: To validate a continuously variable and detailed scoring system to support studies of graft optimisation.
Materials and Methods: The ELF Score was previously derived from routine data (n = 169 patients), then validated in a study of severe graft dysfunction (Currie et al., ESOT 2015). Briefly, regression was used to derive Z scores describing changes in Prothrombin time, bilirubin and lactate. Scores were averaged and translated (score 1–100, with 100 being the best) with a mean of 50 and a standard deviation of 34.1. To assess utility in liver optimisation, data were collected after DCD liver transplantation, in which 14 grafts were retrieved with normothermic regional perfusion (NRP), and 45 contemporaneous grafts were retrieved with standard DCD techniques.
Results: Donor ages in DCD (46; 17–68) and NRP (51; 28–69) groups were comparable, as were functional warm ischaemic times (DCD; 21; NRP; 23 minutes) and recipient ages (DCD; 60; 43–72; NRP; 62; 54–74). At 6, 12, 18 and 24 hours after transplantation, ELF scores in the DCD grafts were 53.1 ± 3.5, 47.8 ± 3.7, 49.3 ± 3.7 and 50.0 ± 4.0. In the NRP grafts, the corresponding scores were 59.2 ± 5.1, 62.7 ± 4.7, 64.7 ± 4.0 and 66.0 ± 4.6. These differences showed a significant enhancement ($p < 0.05$) at all time points from 12–24 hours in NRP grafts.
Conclusions: The ELF score is derived from changes in Bilirubin, Prothrombin time and lactate. Scores above 50 indicate function above average. NRP caused a significant increase in the ability of liver grafts to normalise post-operative liver dysfunction. The data also showed that the ELF Score could

	Peak INR	Peak SGOT	Peak SGPT	Bilirubin day 1	Biliary complications	Vascular complications	EAD
SCOT ($n = 58$)	4.4 ± 2,3	2514 ± 2535	1444 ± 1362	118 ± 109	28%	14%	56%
HTK ($n = 26$)	4.2 ± 1.0	2324 ± 3083	1596 ± 1921	95 ± 73	23%	27%	46%
CEL ($n = 220$)	3.4 ± 1.3	1860 ± 2971	1086 ± 1317	105 ± 85	18%	10%	38%
UW ($n = 206$)	3.1 ± 0.9	1426 ± 2001	939 ± 976	92 ± 78	18%	12%	38%
IGL-1 ($n = 293$)	3.2 ± 1.4	1440 ± 1575	995 ± 1095	107 ± 93	22%	11%	35%

demonstrate differences in graft optimisation as early as 12 hours post transplant.

Translational Liver Ischemia-Reperfusion and Preservation

BOS165 CONTROLLED OXYGENATED REWARMING UP TO NORMOTHERMIA FOR PRE-TRANSPLANT RECONDITIONING OF LIVER GRAFTS

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Background: Controlled oxygenated rewarming (COR) during ex vivo machine perfusion was found to improve organ integrity and limits reperfusion induced tissue injury upon graft implantation (1). Originally, grafts were warmed up to only 20°C but rewarming up to normothermia might add further benefits and provide better prediction of post transplantation organ function.
Methods/Material: Rat livers were retrieved 30 min after cardiac arrest. After 18 hours of static storage at 4 °C the effect of 90 min of oxygenated machine perfusion with Aqix RS-I (a novel extracellular type solution with constant buffering capacity across the temperature range) combined with gentle rewarming up to 20°C (COR20) or 35°C (COR35) was studied and compared with simply cold stored grafts (CS, n = 6, resp).

Post-preservation recovery was evaluated upon warm reperfusion using an established in vitro system. Liver function was assessed by energetic status (ATP), bile production, enzyme release (ALT) and histological tissue morphology.
Results: COR generally resulted in significantly improved energetic recovery, increased bile flow, less ALT release and improved histopathology upon reperfusion as compared to only cold stored livers. However, in spite of tendentially better results after COR20, no significant differences were disclosed between COR20 and COR35. Parameters obtained during COR, especially during COR35, also allowed for prediction of hepatic recovery upon reperfusion. For instance ulterior bile production upon reperfusion was found closely correlated to bile flow observed already during COR35 ($R2 = 0.91$).
Conclusion: COR significantly improved liver quality after static cold storage. Elevation of machine perfusion temperature up to 35°C instead to only 20°C did not further enhance ulterior liver recovery, but seems to be a promising approach to refine ex-vivo evaluation of the graft prior to transplantation.

(1): Am J Transplant, 2013; 13:1450–60.

BOS166 HOPE FOR FATTY LIVER GRAFTS

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Background: Pretreatment of marginal organs by perfusion is a promising opportunity to consider more organs for transplantation. Protection of human DCD (donation after cardiac death) livers by a novel machine perfusion technique, hypothermic oxygenated perfusion (HOPE), was recently established. Here we tested in a rodent transplant model, whether HOPE is also useful for fatty liver grafts.
Methods: Rats were fed over 3 weeks with a special Methionine-Choline-Deficient-Diet (MCDD) to induce severe hepatic macrosteatosis (≥60%). Afterwards, livers were transplanted with either minimal or 12 h cold storage. Additional liver grafts were treated after 12 h cold storage with 1 h HOPE before transplantation. Graft injury after orthotopic liver transplantation (OLT) was assessed in terms of oxidative stress, DAMP release, toll-like-receptor-4 activation, cytokine release, endothelial activation, and the development of necrosis and fibrosis. In addition, we link experimental results with our clinical transplantation of fatty liver grafts analyzing the impact of HOPE prior to liver transplantation.
Results: Implantation of cold stored macrosteatotic liver grafts induced massive reperfusion injury after OLT, compared to controls (non-fatty livers). HOPE treatment after cold storage did not change the degree of steatosis itself, but decreased markedly reperfusion injury after OLT, as detected by less oxidative stress, less nuclear injury, less Kupffer- and endothelial cell activation, and also less fibrosis within 1 week after OLT. Protective effects were lost in the absence of oxygen in the HOPE perfusate. HOPE treatment of severely fatty human liver grafts resulted in immediate function and significant lower complication rate compared to untreated, cold stored controls.
Conclusion: HOPE after cold storage of fatty livers prevents significantly reperfusion injury and improves graft function, comparable to the effects of HOPE in DCD livers and DCD kidney.

Clinical Liver Ischemia-Reperfusion and Preservation

BOS167 NORMOTHERMIC MACHINE PERFUSION: A COST-EFFECTIVENESS ANALYSIS ON A SINGLE CENTER SERIES OF 9 CASES

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Introduction: Normothermic machine perfusion (NMP) for liver transplantation is a novel technique that has been used in a few transplant centers. One of the concerns related to the use of this technology are the costs. The aim of our study is to analyze what is the impact of this technique on costs of liver transplantation (LT).
Methods: We conducted a retrospective analysis on a series of 9 LT patients receiving a graft perfused with NMP at our institution. The device was developed and used under an FDA regulated and IRB approved clinical trial. Patients were matched with SCS preserved historic controls with a 1:2 ratio based on age, calculated MELD score, Donor Risk Index (DRI). Costs that were independent by preservation technique were not included. Costs related to NMP components and assembly have been annualized calculating a hypothetical number of 40 LTs for 10 years.
Results: Every NMP case costed additional $250 for NMP components, $6500 for disposable and perfusate, $281 for a perfusionist. Total expense/case was $20878,22 for NMP and $21052,77 for SCS. Costs are on Table 1.
Conclusion: This single center analysis shows that NMP, which is associated with higher preservation costs, may provide significant cost savings resulting from a superior graft preservation. However study suggests that the superior preservation outcomes may potentially offset and even overcome the higher preservation costs associated with this new technology.

Variable	NMP (9) cost in USD	SCS (18) cost in USD	p
PLT	672.22 ± 601.09	3575 ± 5465.11	0.03
PRBC	1283.33 ± 857.32	1963.89 ± 1898.66	0.21
FFP	222.2 ± 238.63	488.8 ± 538.94	0.08
OR	5530.56 ± 2161.04	6297.22 ± 1486.53	0.28
ICU	1916.67 ± 1285.73	3450 ± 5508.14	0.42
Hospital stay	4222.22 ± 1563.47	5277.78 ± 2539.23	0.26
Total	20878.22 ± 4342.58	21052.77 ± 11889.88	0.95

Clinical Kidney Other

BOS168 THE EFFECT OF MORBID OBESITY ON OUTCOME AFTER KIDNEY TRANSPLANTATION

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Morbid obesity has a significant impact on perioperative morbidity after kidney transplantation. These patients have higher incidence of wound complications, metabolic disorders and longer hospital stay. We sought to determine the rate of perioperative complications and survival among morbid obese (MO) patients after kidney transplantation at our center
Patients and Methods: We searched our database for MO patients (>35 BMI) undergoing kidney transplantation between 2003–2016. The following outcome parameters were analyzed for the whole cohort (n = 46) and then compared between recipients of a kidney from deceased donors (DD=22 and live donors (LD=24): Length of hospital stay, early (<30 days) and late complications as well as patient and graft survival.
Results: Out of 1250 patients having a complete data for analysis we identified 46 patients with BMI>35 (35–45.3); 26 males and 20 females. The median follow up was 36.5 months (7–156 months). The mean recipients age was 54.9 (15–72 years. There was no mortality during the immediate post-operative period; however, 6 patients died at 9–73 months after transplant. The causes for death included: sepsis (4), cardiac (1) and unknown reason (1). Another 3 patients lost their graft immediately post-transplant due to graft thrombosis (1) and PNF (2). DGF requiring dialysis was noted in 17 patients (37%); 15 in the DD group and 2 in the LD group. Early and late complications are listed in the table below. Overall 1- and 5 yr. graft survival were 86.2% and 76.7%, respectively. In the LD group the overall 5 yr. graft and patient survival

were 100%; in the DD group the 5 year graft and patient survival were 53.9% and 66.8%.
Conclusions: Deceased donor transplantation in morbidly obese patients constitutes a high risk for delayed graft function/ non-function and associated with significant morbidity and mortality. Alternatively, elective live donor kidney transplantation seems to be a safe and a better option.

Early Complications< 30 days		Late Complications> 30 days	
Wound	7	Lymphocele	1
UTI	5	UTI	15
MI	3	MI	3
Sepsis	2	Sepsis	2
Urine Leak	1	Ureter Stricture	2
		Pneumonia	3
Total	18 (in 16 patients)		26 (in 23 patients)

BOS169 SURVIVAL IN OLDER KIDNEY RECIPIENTS ADMITTED TO INTENSIVE CARE EARLY AFTER TRANSPLANTATION

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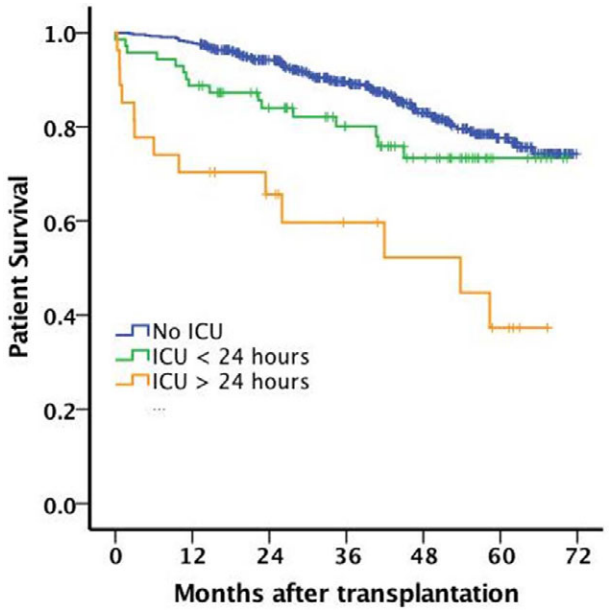
Introduction: Recipients accepted for kidney transplantation (KTx) are getting older and carry more co-morbidities. A challenge is to select the recipients whom will survive the transplantation without major complications and thereby benefit from KTx. We investigate whether a pre-transplant comorbidity score (Liu Comorbidity Index; LCI) may predict early admission (40 days post-transplant) to Intensive Care Unit (ICU), and predict post-operative mortality in kidney recipients older than 55 years.
Method: All patients 55 years and older who underwent KTx at our center between 2011 and 2015 were included. Pre-transplant LCI was registered as part of the routine workup. Post-transplant survival data were extracted from the Norwegian Renal Registry and ICU admission data were retrieved from the patient records. Survival was compared between patients not admitted to ICU, patients who stayed less than 24 hours, and patients who stayed more than 24 hours in the ICU.
Results: Among 640 KTx recipients, 98 were admitted to ICU during the first 40 days post-operative, the majority (63%) within 24 h. Thirty-seven recipients stayed for >24 hr. Respiratory failure was the main reason for ICU admission. Mechanical ventilation was needed in 19, inotropic drugs in 19 and hemodialysis in 18 patients. Median LCI was 2 in the non-ICU group, 3 in the ICU < 24 h ($p = 0.002$ vs. non-ICU), and 4 in the ICU > 24 hr ($p = 0.002$ vs. non-ICU). Survival was significantly impaired in patients who stayed > 24 hr in the ICU compared with patients who stayed < 24 h ($P = 0.007$) and patients not admitted to the ICU ($P < 0.001$) (figure 1). High LCI score was significantly associated with increased risk of ICU admission and lower 5-year survival rate (table 1).
Conclusion: Recipients staying in ICU > 24 h had higher pre-transplant CI and significantly lower survival compared with the two other groups. High LCI score was associated with increased risk of ICU admission and impaired survival

ICU admission	N	OR (95% CI)	P-value
LCI score 0–3	437	ref	ref
LCI score 4–6	151	2.41 (1.44–4.00)	0.001
LCI score ≥ 7	52	3.56 (1.79–7.09)	<0.001
ICU > 24 hours			
LCI score 0–3	437	ref	ref
LCI score 4–6	151	2.59 (1.06–6.37)	0.038
LCI score ≥ 7	52	4.08 (1.33–12.51)	0.014
Survival		5-year survival rate	Log Rank P
LCI score 0–3	437	81%	ref
LCI score 4–6	151	66%	0.001
LCI score ≥ 7	52	61%	<0.001



BOS170 OLDER RECIPIENTS HAVE IMPROVED HEALTH RELATED QUALITY OF LIFE ONE YEAR AFTER KIDNEY TRANSPLANTATION

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Background: A successful kidney transplantation (KTx) is the optimal treatment for patients with end stage renal disease (ESRD). Many older patients experience good health-related quality of life (HRQoL) in modern dialysis, and immunosuppressive drugs are known to have side effects with negative impact on HRQoL. There is a lack of knowledge regarding the effect of KTx on HRQoL in older patients with ESRD. The aim of this study was to measure HRQoL longitudinally in patients ≥65 years of age, from time of enlisting for KTx and until 1 year post transplant.
Methods: Single center prospective study including patients ≥65 years at enlisting for KTx. Participants were asked to complete the Kidney Disease Quality of Life Short Form version 1.3 questionnaire at enlisting and thereafter every 6 months until KTx, withdrawal or death. Post-transplant, the patients received a new form after 10 weeks, 6 months and 1 year. All patients revived prednisolone, tacrolimus and mycophenolate mofetil.
Results: A total of 289 patients were included. By end of January 2017, 102 patients had been transplanted and completed the 1 year post-transplant questionnaires. Mean age at enlisting was 71 years (65-82), 75% male, 28% were not in dialysis and 23% got a kidney from a living donor. The majority of the patients (63%) had low baseline Liu comorbidity (score ≤3).

When comparing the last HRQoL scores pre-tx with 1 year post-tx,

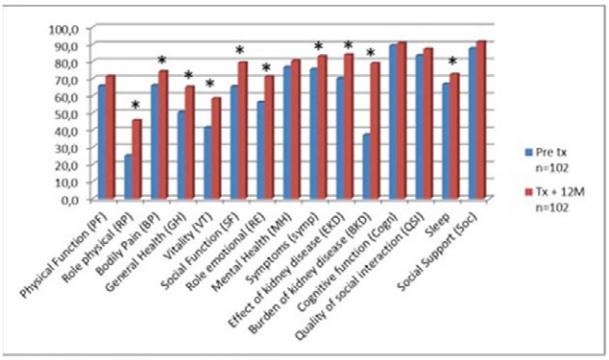

Figure 1; Observed HRQoL, mean values. *p<0.05

	Baseline (n = 102)	Last pre Tx (n = 102)	Tx + 10 weeks (n = 89)	Tx + 6 months (n = 88)	Tx + 1 year (n = 102)	P-value (Pre tx and Tx+1 y
Physical Function	67.7	65.9	70.9	72.6	71.4	0.06
Role Physical	28.3	25.3	27.8	37.8	45.8	<0.001
Bodily Pain	66.6	66.2	73.3	73.7	74.3	0.038
General Health	50.7	50.4	71.5	68.4	65.2	<0.001
Vitality	43.8	41.6	55.5	59.3	58.5	<0.001
Social Function	73.3	65.5	63.2	65.5	79.5	<0.001
Role Emotional	59.6	56.5	55.1	65.5	71.2	0.014
Mental Health	78.2	76.8	82.2	83.5	80.4	0.148
Symptoms	77.4	75.6	83.2	85.0	83.1	<0.001
Effect of Kidney Disease	73.1	70.2	82.4	86.0	84.1	<0.001
Burden of Kidney Disease	40.6	37.3	64.4	71.8	79.0	<0.001
Cognitive Function	91.4	89.4	89.2	92.1	90.7	0.636
Quality of Social Interaction	83.1	83.7	83.2	87.6	87.3	0.063
Sleep	67.4	67.1	67.8	72.0	72.6	0.044
Social Support	88.6	87.7	86.3	92.3	91.7	0.138

BOS171 EFFECT OF VASOACTIVE THERAPY USED FOR BRAIN DEAD DONORS ON GRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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Background:: Serum catecholamine levels and peripheral vascular resistance decrease after brain death. Vasoactive drugs are used in order to control these hemodynamic changes and to improve perfusion of the organs. These drugs might have a role in rejection or loss of the graft organ. We aimed to investigate the effects of vasoactive drugs used in the cadaveric donor care on post-transplant renal graft functions.
Methods: Medical records of 135 cadaveric donors and recipients of the kidneys were evaluated. Correlation analysis was done to assess the data that may cause rejection and graft loss.
Results: From 106 donors, 207 kidneys were harvested. Rejection of the graft occurred in 17.4% of patients and graft loss was seen in 10.3%. Mean age of the 106 donors was 43.6 years. Thirty - five donors (33%) were marginal while consisting 63% of the graft loss. Rejection and graft loss were seen in five out of 16 deceased patients.

The rate of complications among recipients was 41,9% and the mortality rate was 7,8%. Vasoactive drug (Noradrenaline 49%, Dopamine 60%, Adrenaline 3%, Dobutamine 11%) consumption ratio was 85,8% in donor care. Increased number of noradrenaline infusion days was associated with decreased rates of graft rejection and graft loss. This correlation was not found for dopamine.

For 27,4% of the radiologic investigations radiopaque dye was used, and its usage was associated with diminished graft rejection.

	n	P value	Pearson Correlation Coefficient
Rejection			
Number of days noradrenaline used	184	0.008	-0.195
Tests confirming brain death diagnosis	184	0.005	-0.207
Use of radiopaque dye	184	0.029	-0.161
Graft loss			
Number of days noradrenaline used	184	0.046	−0.147
Rejection in the other kidney of the same donor	32	0.033	0.378
Tests confirming brain death diagnosis	184	0.001	−0.238
History of previous rejection	184	0.001	0.74

Conclusion: Noradrenaline but not dopamine usage decreased the graft rejection rate and graft loss, presumably by improving hemodynamic stability and organ perfusion. Confirming tests for diagnoses of brain death may buy time by accelerating the diagnosis and may decrease graft rejection rate. Using radiopaque dye decreased graft rejection rate, but had no correlation with graft loss.

Istanbul region consists an important portion of all the donations done in Turkey thus the result of the study will help us improve the management of cadaveric donors.

BOS172 FACTORS AFFECTING MEDICATION NON-ADHERENCE AMONG KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Adherence to therapeutic recommendations is necessary to obtain optimal medical treatment effects. Medication non-adherence (MnA) can be considered as an interaction of socio-economic, psychological and health-care system related factors. The aims of the study were to assess the level of medication adherence (ME) among our kidney transplant recipients and to identify potentially modifiable risk factors and their associations with MnA.
Materials and methods: A cross-sectional study was performed in 50 living donor kidney recipients (male 27, mean age 39 + 8 years) at least 6 months after the surgery. 19 recipients were employed, 32 married and only 10 with university degree. The participation in the study was voluntary and anonymous. ME was assessed by using the 8-item self-reported Morisky Medication Adherence Scale (MMAS-8). In addition, all participants in the study were evaluated with the 12-item Multidimensional Scale of Perceived Social Support (MSPSS) and Beck Depression Inventory (BDI). Data on patients' demographic, socio-economic and living status, information about recipient's lifestyle and habits were collected using a non-standardized questionnaire.
Results: The majority of recipients (71%) reported high ME, while 23% revealed only medium level of compliance. The remaining 6% scored between 3 and 8 on the 8-point MMAS, were patients with low ME. Among demographic factors involved in the MnA, we confirmed a lower socio-economic status ($p < 0.019$) and lower educational level ($p < 0.02$). The association of MnA with increased depression ($p < 0.01$) and active smoking ($p < 0.003$) was confirmed to. Further data analysis revealed a significant correlation between MnA and lower social support ($p < 0.0001$).
Conclusion : Our study confirmed than approximately 30% of the kidney recipients reported not satisfied level of ME transplantation. A lower socio-economic status, lower educational level, active smoking, increased depression and lack of social support.

BOS173 IS THE CLINICAL OUTCOME GOOD OR BAD IN PATIENTS HOSPITALIZED WITHIN 1 YEAR AFTER KIDNEY TRANSPLANTATION?

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Background: Although kidney transplantation (KT) is the best treatment for end-stage renal disease, the hospitalization rate at early period of KT is still high. Nevertheless, the association between the hospitalization within 1 year after KT and graft survival is unclear. We investigated the incidence and causes of hospitalization, and clinical outcome of the patients hospitalized within 1 year after KT.
Methods/Materials: We retrospectively analyzed the kidney transplant recipients (KTRs) hospitalized within 1 year after KT between 2013 and 2015.
Results: Of the 174 patients who received KT during the study period, 48% patients were admitted within 1 year after KT, and the number of hospitalizations was 116. The mean time from KT to 1st hospitalization was 4.2 months. Among them, 78% were hospitalized for medical causes and 22% were hospitalized for surgical causes. The most common cause was cytomegalovirus infection (CMV) (25%), followed by urinary tract infection (17%), and acute rejection (13%). The ages of recipient and donor in the hospitalized group

were significantly older than the non-hospitalized group. The rate of deceased donor KT, acute rejection, more than 50% panel reactive antibody, and positive donor specific antibody was significantly higher in the hospitalized group than in the non-hospitalized group. In Kaplan-Meier analysis, graft and patient survivals were significantly worse in the hospitalized group than in the non-hospitalized group.
Conclusion: The incidence of KTRs hospitalized within 1 year after KT was high. Most causes of hospitalization within 1 year after KT were CMV infection, urinary tract infection, and acute rejection. In KTRs with high immunologic risks, the hospitalization rate by rejection is high and the hospitalization rate by infection is also high due to the strong immunosuppression to prevent rejection. Therefore, the immunosuppression status of these patients should be closely monitored to reduce the hospitalization rate.

BOS174 CLINICAL CORRELATION OF WARM ISCHAEMIA TIME WITH DELAYED GRAFT FUNCTION IN CADAVERIC KIDNEY TRANSPLANT

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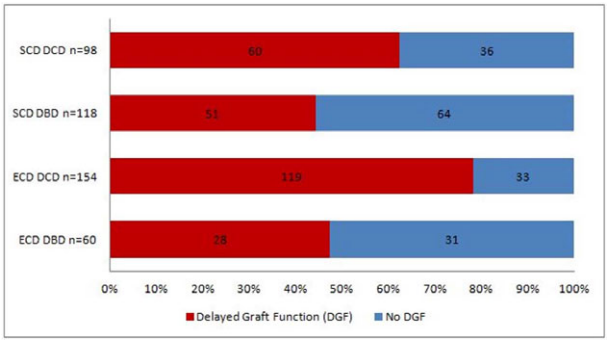
Prolonged second Warm Ischaemia Time (WIT) (anastomosis time) is considered to have impact on early kidney graft function after transplantation as suggested in some clinical data. In this study we evaluated impact of WIT on incidence of delayed graft function (DGF) in deceased donor kidney transplant.
Methods: Retrospective review of prospectively collected data for all the patients undergoing cadaveric kidney transplant from January 2010 to August 2015 was done. Clinical correlation of WIT (in minutes) in the recipient with graft function at the end of 1 year was analyzed.



Results: A total of 436 patients underwent cadaveric kidney transplant; ECD-DBD=60, ECD-DCD= 154, SCD-DBD=118, SCD-DCD=98. 78.3% of the ECD-DCD and 62.5% SCD-DCD had DGF (as compared to 47.5% ECD-DBD and 44.3% SCD-DBD; p = 0.0005). Subsequently we divided all four groups to DGF and non-DGF subgroups and compared correlation between WIT and outcomes: DGF vs. non-DGF ECD-DBD n = 28 vs. 31; ECD-DCD n = 119 vs. 33; SCD-DBD n = 51 vs. 64; SCD-DCD n = 60 vs. 36. There was no statistical difference in mean WIT between DGF subgroups (47.1 min in ECD-DBD, 48.4 min in ECD-DCD, 49 min in SCD-DBD and 47.3 min in SCD-DCD; p = 0.885); nor in non-DGF subgroups (48.7 min; 50.2; 45.9; 48.7 respectively; p = 0.885). However, SCD DBD-DGF subgroup had 2.1 min longer WIT compared to SCD-DBD non-DGF subgroup (49 vs. 45.9; p=>0.5), which was largest difference between DGF and non-DGF same donor type subgroup.
Conclusions: WIT does not seem to have a clinical correlation to graft function in our study. Greatest impact of prolonged WIT on early graft function are in SCD-DBD kidneys; in ECD and DCD kidneys there are multiple other factor with negative impact on early outcomes. Therefore, a study in live donor kidney transplants looking at the impact of WIT on graft function would give us more information of the effect of WIT on DGF, where donor factors affecting the graft function have been excluded.

Total number of participants n = 436	ECD DBD	ECD DCD	SCD DBD	SCD DCD	Significance
Delayed graft function group, n = 262					
% age of Donors	47.5%	78.3%	44.3%	62.5%	0.0005
Mean Recipient Age (Years)	59.6	62.9	47.1	54	
Mean Donor Age (Years)	63.9	67.5	42.1	44.0	
Mean 2nd Warm Ischaemia Time (in minutes)	47.1	48.4	49	47.3	0.885
Non delayed graft function group, n = 164					
Mean 2nd Warm Ischaemia Time (in minutes)	48.7	50.2	45.9	48.7	0.885

BOS175 THE EFFECT OF RECIPIENT BMI ON RENAL TRANSPLANT OUTCOMES

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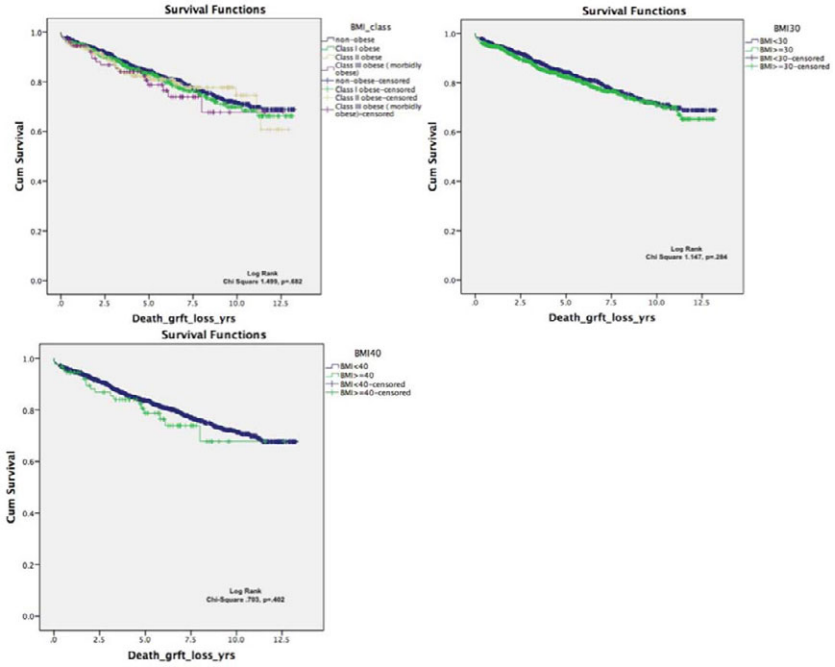
Background: Purpose of the study was to explore the effect of BMI class on renal transplant outcomes. Method: Single center retrospective analysis of deceased and living donor renal transplants performed through period 07/2003–07/2016. The cohort was divided into 4 BMI categories: non-obese,



Class I, II and III obese (morbidly obese). Outcomes were graft survival, DGF, rejection, 1-year eGFR and length of stay (LOS).

Results: N = 2424 patients. Median recipient BMI was 28 kg/m2. 40.1% of the recipients were obese (BMI≥30 kg/m2) and 3.8 % Class III obese (BMI≥40 kg/m2). Higher BMI recipients received lower KDPI kidneys (p = 0.002). Obese recipients had higher DGF rates and lower 1-year eGFR (p = 0.006). LOS and rejection rates were similar. Also, graft survival was similar across all BMI groups, as well as among obese vs. non-obese and between BMI≥ 40 (Class III or morbidly obese) vs. BMI<40 mg/m2 patients.

	<30	30–34.9	35–39.9	≥40	
BMI (kg/kg/m2)	Non-obese	Class I obese	Class II obese	Class III obese	p
n (%)	1453 (59.9)	593 (24.5)	285 (11.8)	93 (38)	<.001
Living donor (%)	44.7	41.8	38.2	50.54	.087
KDPI (mean+-SD)	0.54 + -0.275	0.51 + -0.274	0.52 + -0.235	0.42 + -0.21	.002
DGF (%)	23.3	28.7	37.9	30.1	.000
1 year rejection (%)	15.3	15.0	16.8	19.4	.959
1-year GFR	60.06 ± 21.242	58.55 ± 18.768	54.72 ± 16.619	58.29 ± 22.189	.006

Conclusion: With appropriate donor and recipient selection, obese and morbidly obese patients have acceptable outcomes after kidney transplantation and should not be excluded for transplant based on BMI criteria alone.

BOS176 PREDICTING CLINICAL OUTCOME IN THE ELDERLY KIDNEY TRANSPLANT RECIPIENTS

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Introduction: The incidence of End Stage Renal Disease is highest in older adults, which become the fastest growing group of kidney transplant (KT) candidates in recent years. Outcomes in this population have not been fully defined. The purpose of this study was to evaluate graft and patient survival in elderly KT recipients and to identify risk factors that predict outcomes.

Methods: We retrospectively analyzed patients aged 65 years and older who underwent primary KT between 1995 and 2016 in our center. Outcome measures were: donor and recipient age and gender, time on dialysis, renal disease etiology, cold ischemia time, HLA-mismatch, delayed graft function, acute rejection, and hospitalization length. The predictors of graft and patient survival were analyzed using Cox regression analysis.

Results: In a total of 1988 KT, 94 (4.7%) were in patients aged ≥ 65 years. Their mean age was 67.5 years, 61.7% male, 96.7% from deceased donors. During a median follow-up of 13.8 ± 2.5 years, 20.2 % of patients died, 57.2% due to cardiovascular causes and 25 patients lost their KT, 19 (76.0%) of them due to death with a functioning graft. The 1- and 5-year patient survival rates were 92.1% and 80.3%, respectively. Longer dialysis time is a risk factor for death at 1- (HR: 1,128, 95% CI [1,044; 1.219]) and 5-year (HR: 1.123, 95% CI [1.045; 1.206]). Acute rejection during the first year (HR: 3.936, 95% [1.094; 14.168]) is a risk factor for death at 5-year. The 1- and 5-year death-censored graft survival rates were 97.8% and 94.2%, respectively. None of the outcomes measures studied were independent risk factors for graft failure.

Conclusions: KT in patients aged 65 years and older is associated with excellent patient and graft survival, and age alone should not preclude this treatment. Longer dialysis time and acute rejection are independent risk factors for patient death, representing potential targets for interventions aimed at improving outcomes survival in elderly KT recipients.

BOS177 AN EVALUATION OF SARCOPENIA IN KIDNEY TRANSPLANT PATIENTS

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Background: Sarcopenia is a state of degenerative skeletal muscle wasting, and has recently been recognized as an important physiological change that associated with poor physical condition, more frequent conditions, and poorer patient survival. But the clinical information of sarcopenia in kidney transplantation (KTx) remains limited.

Methods: During the period between April 2015 and January 2017, we retrospectively evaluated consecutive 187 patients undergone KTx at our department. Computed tomography (CT) images were used to calculate each patient's skeletal muscle index, an indicator of whole-body muscle mass. Sarcopenia was defined according to the sex-specific definitions, based on the patient's skeletal muscle index and body mass index. CT was performed prior to transplant and at 1 year post-transplant. Change in sarcopenic status according to KTx was analyzed.

Results: Overall 141 patients were enrolled. Skeletal muscle was increased in 75 patients (53.2 %) after transplant. Prior to transplant, 45 patients (31.9 %) were sarcopenic status, and sarcopenia was cured in 24 patients (17.0 %). These patients were significantly associated with younger age, shorter dialysis duration and male. Meanwhile, graft function at 1 year post-transplant was not associated with improvement of sarcopenia.

Conclusions: KTx can improve patient performance status.

BOS178 KIDNEY TRANSPLANTATION IN PATIENT WITH JEUNE SYNDROME

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Introduction: Jeune syndrome (asphyxiating thoracic dystrophy, ATD) is a rare autosomal recessive skeletal dysplasia. Progressive kidney disease, the nephronophthisis occurs in about 30% of patients. There are several cases of patients with Jeune syndrome treated with kidney transplantation successfully described in the literature.

Methods: Case report study.

Results: Male patient, diagnosed with Jeune syndrome in the age of two. He has narrow thorax with short, broad, horizontally oriented ribs, a typical trident appearance of the acetabular margins, small thorax, brachydactyly, short and broad diaphyses, and wide metaphyses of the arms and legs, and short iliac bones. He was diagnosed with retinitis pigmentosa, complicated cataract of the right eye. Also diagnosed with pancreatic cysts. Treated with recombinant growth hormone. In the age of three had several episodes of seizures, controlled with anticonvulsants. Radiological examination in the age of two years also showed nephronophthisis. He developed CKD with arterial hypertension and renal anemia in the age of five. Treated with intermittent hemodialysis for eight months without complications. Treated with living related kidney transplantation, father was kidney donor. Treated with basiliximab in induction and with immunosuppressive protocol including cyclosporine, mycophenolate mofetil and steroids. The kidney transplantation was without complications. There was no DGF - delayed graft function, acute rejection or other complications, with remaining arterial hypertension. He was evaluated thirteen years after transplantation. The level of serum creatinine was 123 mcmol/l, with creatine clearance of 0.96 ml/s, and proteinuria level of 0,82 gr, with anemia controlled successfully with ESA. Respiratory function tests showed general restrictive ventilation disorder, but still well tolerated.

Conclusions: ATD is multi organ disease with variable expression, with CKD progression treatable with kidney transplantation.

BOS179 DO EXTENDED CRITERIA DONOR AND DONOR VASCULAR DISEASE INCREASE THE RISK OF RENAL ARTERY STENOSIS?

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Introduction: Renal artery stenosis (RAS) remains the most common vascular complication after transplantation. Early RAS (<6 months) is associated with graft-specific and operative factors. The increased use of extended criteria donor (ECD) kidneys may contribute. We aimed to correlate early RAS and associated graft quality.

Method: Retrospective analysis of early RAS cases (angiography confirmed; 01/15–09/16) at a single centre was performed. Data was collected and assessed for donor, graft and recipient factors, including arterial quality.

Results: 15 (2.98%) cases of RAS were identified from a total of 504 transplants (333 deceased donors (DD); 171 live donors (LD)). There were 11 DD RAS (3.3%) with 4 in LD (2.3%). Mean donor age was 53.1 years (range 13–69), with a mean total ischaemic time (TIT) of 920 minutes (1169 and 239 for DD and LD). The mean number of days to RAS was 72.5 (range 23–107). 11 (73%) stenoses were ostial and 4 (27%) post-anastomotic. Each of the 4 LD cases had ostial stenosis. 7 DD (64%) recipients had ostial stenosis and 4 (36%) had mid-arterial stenosis. DD's also developed ostial RAS despite the use of a Carrel patch (9/11 cases). Reasons for patch sacrifice included retrieval injury and severe atheromatous disease. Donor arterial quality was

reported as healthy to mildly diseased (72.8%), and moderately to severely diseased (27.3%) All 15 underwent balloon angioplasty with subsequent improvement in graft function.
Discussion: This series represents an increase in incidence of deceased donor RAS. The ostial stenosis in LD recipients has previously been reported and has been associated with anastomotic stricture. However, in DD, donor arterial disease, the increased rate of ECD's and prolonged TIT, may explain increased rates of early RAS. With more marginal organs being accepted, complication rates including early RAS are likely to continue to rise. The impact on late RAS and overall transplant outcome requires further investigation.

BOS180 EFFECT OF RENAL CORTEX VOLUME ON POSTOPERATIVE GRAFT FUNCTION. DOES IT REALLY MATTERS?

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Background: Renal volume is considered an important factor contributing to grafts quality and postoperative kidney graft function. Low renal mass may imply low nephron mass and lower GFR. In this study we aimed to evaluate the effects of donor cortex volume on postoperative renal function in kidney transplant (KTx) recipients.
Material and methods: A consecutive sample of 65 kidney tx recipients (41 males and 23 females, mean age: 37 ± 11 years) were enrolled in this study. Donor kidney cortex volume (DKCV) was measured by computed tomography and estimated glomerular filtration rate (eGFR) of the recipient was calculated on postoperative (postop) 7th day and on last follow up using the CKD-EPI formula. The patients were divided into 4 subgroups, Group 1: male-male KTx, Group 2: female-female KTx, Group 3: female-male KTx, and Group 4: male-female KTx. The effects of pre-KTx donor kidney cortex volume on allograft functions were evaluated.
Results: The median post-transplant follow up was 21,5 (IQR 12–35) months. Postop 7th day and last day follow-up of donor eGFR was 73 ± 6 mL/min and 70 ± 3 mL/min, respectively. DCKV was not correlated with recipients eGFR of postop 7th day and last follow-up. No significant correlation was found between donor gender, eGFR and recipient's eGFR on postop 7th day and last follow-up. In a subgroup analysis there was only correlation of transplanted renal volume and recipients' postop 7th day serum creatinine in Group 3 ($r = 0.405$, $p = 0.49$). Other subgroups did not reveal any significance.
Conclusion: Although DKCV did not have significant impact on early and mid-term post-KTx allograft outcomes, multiple post-KTx factors including infections, rejection episodes and treatments may dilute the desired influence. Therefore, pre-KTx DKCV should not be considered alone as a reliable tool assessing postop kidney allograft function.

Translational Kidney Other

BOS181 RECIPIENT APOL1 GENOTYPE AND ALLOGRAFT OUTCOMES IN LIVE KIDNEY TRANSPLANTATION

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Background: Apolipoprotein-L1 (APOL1) risk variants have emerged as a predictor of renal disease in individuals of African Ancestry (AA). The effect of APOL1 risk variants on the Living Kidney Transplant Recipients (KTR) has been rarely reported. We investigated the effect of APOL1 genotype on allograft outcomes.
Methods: We reviewed prospectively collected data on 220 KTR (141 male, mean age 46.7, 18-73 years). Genomic DNA was extracted from stored blood samples and three APOL1 single nucleotide polymorphisms (SNPs) were amplified using primers. The product was sequenced using the forward primer on the ABI 3130xl. The variants typed (rs73885319 and rs60910145) are missense mutations in the last exon of the APOL1 gene (S342G and I384M) and (rs71785313), a six base-pair deletion leading to the deletion of two amino acids (delN388/Y389) in the last exon of the APOL1 gene. Sequences were evaluated using Mutation Surveyor software.
Results: 220 KTR were included, 77 Asian (48 male, mean age 45.9, 20-69 years), 66 AA (37 male, mean age 47.7, 20-71 years), and 77 Caucasian (47 male, mean age 46.65, 18-74 years), with a mean follow up 69+27 months. Two APOL1 risk alleles were found in 28 (42.4%) AA, 1 (1.3%) Asian and none of the Caucasian KTRs. ($p<0.001$) In the AA cohort, Kaplan Meier analysis showed no significant difference in allograft survival in KTRs with >2 and 0-1 risk alleles. (log rank p=0.49) However KTR with >2 risk alleles were found to have lower eGFR at 6m (54.7+18.1 vs 45.3+15.3, p=0.03), 1y (56,7+17.5 vs 44+17.4, p=0.008) and 3y (51.5+21.7 vs 40.9+17.1, p=0.04).
Conclusion: In this single center study, with medium term follow up, the presence of APOL1 risk alleles did not affect allograft loss, but KTR with >2 risk alleles appear to have lower eGFR for the first 3 years post transplant.

Clinical Kidney Surgical Technique

BOS182 CHALLENGING CASES IN HAND-ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY: RIGHT KIDNEYS WITH MULTIPLE ARTERIES

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Background: There are several studies offering hand assisted retroperitoneoscopic (HARP) approach as a better surgical technique for right donor nephrectomy. But the data on challenging situations like multiple arteries is missing in literature. Herein, we review our series of 509 HARP donor nephrectomies with a special emphasis on kidneys with multiple (2 or more) arteries (MA).
Material/Methods: The data on 100 (19.6%) right kidney (RK) donors vs. 409 (80.4%) left kidney (LK) donors who underwent HARP nephrectomy between February 2009 and December 2015 and the data on their respective living donor kidney transplant recipients were retrospectively analyzed.
Results: The incidence of MA was not different in RK (16.0%) vs. LK (16.4%) transplants ($p = 1.0$).

	MA Right (n = 16)	MA Left (n = 67)	P value
Donor age	45.8 ± 15.0	43.7 ± 12.4	0.5
Donor gender (M/F)	6/10	39/28	0.1
Donor BMI	26.7 ± 4.7	26.6 ± 4.4	0.9
Recipient age	31.6 ± 14.5	42.7 ± 12.1	0.003
Donor dissection time (min)	102 ± 44	104 ± 27	0.7
Ischemia time (min)	87.3 ± 29.5	87.8 ± 26.4	0.9
Donor major peritoneal opening (%)	1 (6.3%)	4 (6.0%)	1
Recipient graft loss (%)	0 (0%)	8 (12.3%)	0.3
Creatinine, postoperative day 5 (mg/dl)	1.0 ± 0.4	1.4 ± 1.0	0.01
Creatinine, postoperative month 1 (mg/dl)	1.0 ± 0.2	1.4 ± 1.0	0.01
Creatinine, postoperative month 6 (mg/dl)	1.0 ± 0.2	1.2 ± 0.4	0.03
Creatinine, postoperative month 12 (mg/dl)	1.0 ± 0.2	1.4 ± 1.1	0.04
Follow-up (months)	45.8 ± 15.0	43.7 ± 20.1	0.3
Creatinine on the final visit (mg/dl)	0.9 ± 0.2	1.2 ± 0.5	0.03
Recipient hospital stay (days)	7.5 ± 2.3	8.5 ± 5.2	0.4

There was no difference in terms of 1-year death-censored graft (100% in RK vs. 96.9% in LK, $p = 0.1$) and patient survival (100 % in RK vs. 96.4% in LK, $p = 0.4$) between RK and LK transplantation. In donors with multiple arteries, the reason for selecting RK over the LK were early branching (n = 1), renal artery stenosis (n = 2), nephrolithiasis (n = 4), renal cysts (n = 5), and more than 2 arteries on the right (n = 2). When the whole cohort of 509 patients was analyzed, there was no difference in terms of 1-year death censored graft survival between the RK and the LK transplants (100% in RK vs. 97.9% in LK, $p = 0.6$) and between the grafts with single artery (SA) vs. MA (98.7% in SA vs. 96.3% in MA, $p = 0.1$). None of the donors had conversion to open DN or required readmission. All transplanted kidneys had immediate function. We interpreted the significant difference in post-transplant creatinine levels between the RK and LK transplants using MA as irrelevant, because this difference did not reflect on graft survival.
Conclusion: In LDKT using kidneys with MA, there is no significant difference in terms of donor and recipient outcomes when HARP technique is utilized. The results are excellent even in challenge as RK with MA.

BOS183 OPTIMIZING HAND-ASSISTED RETROPERITONEOSCOPIC LIVING DONOR NEPHRECTOMY (HARP) WITH A PASSIVE POLARIZING THREE-DIMENSIONAL DISPLAY SYSTEM

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Background: Hand-assisted retroperitoneoscopic donor nephrectomy (HARP) needs a high grade of minimal-invasive surgical skills. Expected complications during establishing this technique could hinder its introduction in a transplantation center. Also teaching this operation is challenging. Passive polarizing 3D display technique seems to ease minimal-invasive surgery. Aim of this study was to evaluate the influence of a 3D display system on HARP.
Methods: We performed an observational study after the establishment of the HARP technique in our center. Therefore we compared 81 HARPs performed with a 2D display system vs. 41 HARPs performed with a 3D display system including a learning curve evaluation and matched pair analyses.
Results: Operation time (OT) and warm ischemia time (WIT) were significantly shorter for the 3D-HARPs compared to 2D HARPs (OT 98 $\pm$ 16 min vs. 106 $\pm$ 19 min, p = 0.036; WIT 97 $\pm$ 37 s vs. 120 $\pm$ 57 s, p = 0.015). Blood loss (BL) was not different (52 $\pm$ 37 ml vs. 57 $\pm$ 70, p = 0.71). The matched pair analyses 3D vs 2D (pairs matched for "side of donor nephrectomy" and "arteries >1") with 41 exact matches confirmed this data (OT p = 0.028, WIT p = 0.014, BL (p = 0.79). The learning curves seem also to be optimized by the 3D technique compared to the 2D technique.
Conclusion: The introduction of passive polarizing 3D display technique facilitates the surgical preparation and could help to optimize HARP.

	HARP 3D (n = 41)	HARP 2D (n = 81)	p-value
Operation time (min)	98 $\pm$ 16	106 $\pm$ 19	0.036
Warm ischemia time (s)	97 $\pm$ 37	120 $\pm$ 57	0.023
Blood loss (ml)	57 $\pm$ 70	52 $\pm$ 37	0.710

BOS184 ROBOT-ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY: EXCESS OR OPPORTUNITY?

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Background: Robot-assisted laparoscopic surgery has been widely described in recent years in multiple surgical fields. More and more transplant centers are adopting this technique for living donor nephrectomies. The advantages of laparoscopy are undeniable, but the potential benefits of a robotic technique are not yet clearly defined.
Methods: We analyzed the learning curve and results of this surgical technique in a single University Transplant Center. We compared 46 (5 right, 41 left) sequential robot-assisted donor nephrectomies (RALDN) performed during the past 3 years, with 20 full-laparoscopic donor nephrectomies (LDN). The parameters analyzed were total operating time, blood loss and blood transfusions given, warm ischemia time, pre- and post-operative serum creatinine, and length of hospital stay.
Results: There was no statistical difference between RALDN and LDN in any of the parameters analyzed. No patients developed significant postoperative complications above Clavien-Dindo Grade 2. The number of intraoperative bleeding episodes was comparable, with similar mean blood loss (220 vs 240 ml). The median operating time was similar, 240 minutes (RALDN group: range 160–335), vs 225 minutes (LDN). No procedure was converted to open. The median warm ischemia time was identical (6 minutes). The difference between pre- and post-operative serum creatinine levels was not statistically significant. Finally, the median length of hospital stay was the same in the 2 groups, 5 days.
Conclusion: RALDN is safe with comparable outcomes to standard LDN technique in our institution. Despite the lack of statistically significant advantages, we believe that RALDN could be extremely beneficial in managing intraoperative complications.

We recognize that utilizing robotic techniques is cost negative compared to LDN. However, considering the ethical importance and financial benefits to society of living donation, we believe that RALDN could be utilized in this scenario.

BOS185 RENAL TRANSPLANTATION IN PATIENTS WITH VOIDING DYSFUNCTIONS AND WITH OBSTRUCTIVE UROPATHY

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Cairo University, Egypt

Introduction: We aimed to evaluate outcomes of KT in OU and VD ESRD patients and assess complications specific to this patient population and their impact on graft function and survival.
Methods: This was a retrospective review of KT database of King Fahd Kidney Transplant Unit of Cairo University, Cairo, Egypt. It included patients who underwent living donor related or unrelated KT for ESRD due to OU and/or VD from January 2007 through December 2011. This included an assessment of procedures needed in optimizing the UT for renal allograft. A number of perioperative patient and disease parameters were also examined.
Results: The study included 25 KT recipients who underwent KT for ESRD due to OU or VD. 24/25 was males. Mean age was 19.3 $\pm$ 7.12 years at time of KT. ESRD was due to neurogenic bladder in 6, posterior urethral valves (PUV) in 5, urethral strictures in 5, urolithiasis in 5, vesicoureteral reflux in 3, and prune-belly syndrome in 1. There were 25 ancillary procedure performed with 5 patients undergoing $\geq$ 2 procedures, either prior to or after KT. Pretransplantation nephrectomy, augmentation ileocystoplasty, fulguration of PUV, VIU and urethroplasty were done in 16, 4, 5, 4 and 1, respectively. Mean follow-up was 24.96 $\pm$ 11.95 months. All patients were alive with functioning grafts at end of last recorded follow-up. Mean serum creatinine (mg/dL) at 3, 6 and 9 months, and 1, 2, 3 and 4 years was 0.99, 1.16, 1.17, 1.14, 1.27, 1.08 and 1.11, respectively. Post-transplantation follow-up revealed UTI in 4 (16%) cases. Age and post-transplantation UTI had a significant impact on serum creatinine at 1 year post-transplantation ($p < 0.04$ and $p < 0.01$, respectively).
Conclusions: KT can be safely performed in patients with ESRD due to OU and VD with acceptable outcomes and graft survival rates. Ancillary procedures may be needed to optimize UT prior to KT. Only age and post-transplant UTI had a significant impact on serum creatinine at 1 but not 2 years following KT.

BOS186 CLINICAL OUTCOME OF A PATIENT OF POST RENAL TRANSPLANT ENCAPSULATING PERITONEAL SCLEROSIS AFTER DUODENAL RESECTION ANASTOMOSIS WITHOUT ADHESIOLYSIS

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We report here a 62-year-old male patient, with past medical history of hypertension, diabetes mellitus, and end-stage renal disease who remained on peritoneal dialysis for 12 years without a single episode of peritonitis. He had living related renal transplant the year 2015. He received ATG induction and was maintained on triple immunosuppressant with Tacrolimus (FK), mycophenolate, and prednisolone. After 3 months of transplant with stable renal parameters the patient started complaining of abdominal bloating, early satiety, anorexia with vomiting and documented weight loss. FK was replaced by cyclosporine with no clinical improvement.

In a time span of one year, the patient had significant weight loss of 15 kg with worsening signs and symptoms. Upper and lower gastroscopy was normal except mild gastritis. Depending upon high clinical suspicion and radiological imaging, exploratory laparotomy was done with primary resection anastomosis of the second part of the duodenum. Surgical findings were highly suggestive of the preoperative diagnosis of Sclerosing peritonitis. This was further consolidated by the typical histopathological findings of small bowel and morphological findings of peritoneum and visceral structures. The histopathological findings of the omentum were fibroadipose tissue with sclerosing hyaline fibrosis with no evidence of malignancy. The patient remained on TPN for a period of three weeks and significantly improved clinically and starts regaining his weight with normal renal parameters.
Conclusion: Post transplant Sclerosing peritonitis is the diagnosis of high clinical suspicion in a patient who had undergone peritoneal dialysis prior renal transplant.

BOS187 NATURAL HISTORY OF SPLENECTOMY IN A CASE OF POST RENAL TRANSPLANT WITH RESISTANT ABO INCOMPATIBLE VASCULAR REJECTION

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Prince Sultan Military Medical City, Saudi Arabia

We report a 38 years old male who had an ABO incompatible renal transplant from his wife. Recipient blood group was O positive and donor was A1 positive. His HLA cross matching was negative with no donor specific antibodies. Anti-A1 titer was 1:64. He received Rituximab followed by 5 sessions of Immunoadsorption (IA) and Intravenous immunoglobulin (IVIG) as desensitization protocol of our renal transplant program. Anti-A1 titer came down to 1:2 after this regimen. He had induction with Anti thymoglobulin (ATG) and methylprednisolone. He had smooth surgical course and brisk urine output.

Renal functions improved progressively and serum creatinine was 111 mmol by fourth post-operative day. Post-transplant he received three sessions of IA however, it was discontinued as Anti-A1 titer became 1:1. After 5 days Anti-A1 titer started to rise, and became 1:32. Despite restarting daily IA along with IVIG, Anti-A1 titer kept on increasing and reached 1:128 with deterioration of renal function and creatinine increased to 236 mmol on day 8 post surgery. Kidney biopsy showed interstitial hemorrhage, focal glomerular and arteriolar thrombi with diffusely positive C4d despite of undetectable donor specific antibodies (DSA). With this histopathological findings diagnosis of ABO antibody mediated acute vascular rejection was made. As patient failed to respond to combined IA, IVIG, ATG we decided to go for Splenectomy as a last anti-rejection resort. Laparoscopic Splenectomy was done on 9th post-transplant day with gradual recovery of renal function and progressive drop of Anti-A titer. Anti-A titer became 1:4 and creatinine dropped to 144 mmol on day 5 post-Splenectomy. He is following in our transplant clinic for last 2 years with maintenance triple immunosuppressive regime and is maintaining creatinine of 110–120 mmol.

Conclusion: Splenectomy can be considered a feasible option in ABO incompatible Transplant with resistant vascular rejection.

BOS188 PRELIMINARY EXPERIMENTAL MODEL FOR "ILEOBLADDER" AND RENAL TRANSPLANT IN RATS AND PIGS

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Introduction: Small, poor compliant or unstable bladders are one of the major problems that we face in patients. Many studies have been performed since more than a century (often unsuccessful or associated with high rate of complications), but no distinct method has been developed. Herein, our goal was to develop and evaluate a new ileobladder model.
Methods: A total of 8 rats (250–300 g) and 3 pigs (approximately 100 kg) were cared for according to institutional and published guidelines. General anesthetic was given and laparotomy was done through midline incision. Ileal loops were prepared for ileobladder. After cystectomy down to 1 cm above trigon, anastomoses were done between antimesenteric sides of ileal loops and the remnant of the bladder with 6/0 prolene suture. In addition, the same procedure was performed simultaneously with renal transplantation in 2 other pigs.
Results: One rat died on the first day of operation due to hemorrhage of multiple organs. Two rats survived for 5 days, 3 rats for 7 days, 1 rat for 11 days, and 1 rat is still alive 32 days after surgery. One pig survived for 22 days, 1 for 9 days, and 1 pig is still alive 15 days after surgery. Of the 2 pigs that received a simultaneous renal transplant, both are still alive and doing well 10 and 6 days after surgery, respectively. Urinary discharge was normal in all of them. Pathological examination of the anastomosis sites reported a normal healing process with moderate inflammation.
Conclusions: Although some complications were faced as no draining procedure was used, in terms of technique, our new ileobladder model is promising for providing functional bladder volume. Based on this preliminary study, we will perform a larger scale series in both an experimental and clinical setting.

BOS189 LONG-TERM ALLOGRAFT AND PATIENT SURVIVAL IS IMPAIRED IN RENAL TRANSPLANT RECIPIENTS RECEIVING ANTIPLATELET THERAPY

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University Hospital Essen, Germany

Background: Antiplatelet therapy is common in patients on the waiting list for kidney transplantation. This study evaluates the incidence of postoperative bleeding in patients undergoing kidney transplantation with antiplatelet therapy and analyzes the impact on the outcome.
Methods: We included all patients in our center undergoing kidney transplantation with concomitant antiplatelet therapy (January 2007 to June 2012). Data were collected by chart review prospectively. Univariable and multivariable logistic regression and cox proportional hazards were performed to identify risk factors for the long-term outcome.
Results: Among 744 kidney transplant patients, 161 (n = 98 male, 60.9%) received oral antiplatelet therapy and were included in the study. One third of patients demonstrated signs of bleeding requiring surgical treatment in 18%. Coronary artery disease, deceased donor kidney transplantation and dual antiplatelet medication were identified as independent risk factors for postoperative bleeding. Postoperative bleeding was identified as an independent risk factor for graft and patient survival. One-year allograft survival in the non-bleeding group was significantly better than in the bleeding group (91.4% vs. 75.9%, p = 0.023), respectively.
Conclusion: This analysis indicates a high risk for bleeding in renal transplant patients under antiplatelet therapy. The associated negative effect on long-term allograft and patient survival underscores the need to reduce any risk factor for postoperative bleeding.

BOS190 RECONSTRUCTION OF A DAMAGED LOWER POLAR ARTERY FOR KIDNEY TRANSPLANTATION USING TUBULARISED DONOR AORTA

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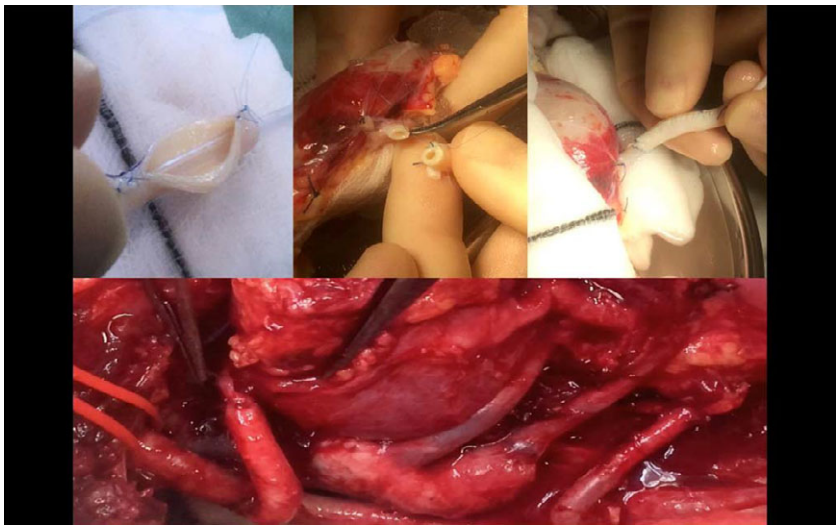
Introduction:
Live donors, extended donor criteria and the maximum usage of organs with anatomical and / or vascular variants are some of the mechanisms use to increase the number of organs available.
Case: We present the case of a kidney transplant, in which the organ had an iatrogenic injury to a lower pole arterial branch occurred during retrieval. Reconstruction was performed using donor's tubularised aortic patch.

The donor, a 35 year old male, who died after cardiac arrest (DCD), Maastricht III. The right kidney was accepted; it had three veins in a single cava patch. Three renal arteries, the main artery with aorta patch 8 cm long. A small lower pole artery which was sectioned during retrieval surgery at approximately 1 cm from its origin and a third small mid-lower pole artery. The ureter had bifid renal pelvis.

During bench surgery the kidney perfused well with Soltran. From the three veins in the single cava patch, the posterior branch was ligated in order to allow the single patch to be more mobile. The small mid-low pole artery was already damaged and was deemed unreconstructable and was therefore tied off. The main artery was left with a 1 cm aortic patch. The lower pole damaged artery



was reconstructed using tubularised aorta patch to a total length of 5 cm. No additional donor vessels had been sent.

The reconstruction was carried out with a 5 cm length Aorta patch. Using an 8 ch Nelaton bladder catheter as a mold a 5 cm long aorta segment was tubularised using 7-0 prolene 3 interrupted stitches in the distal area to avoid stenosis and prolene 7-0 continues suture in the rest of the patch to minimize bleeding risk. After construction of the tubularised aorta, E-E anastomosis to the damaged polar artery was done with interrupted 7-0 prolene.
Conclusion: While the waiting list for a Kidney continues to rise and we continue to have organ shortness, vascular retrieval injury should not be an absolute contraindication for transplant.

BOS192 LAPAROSCOPIC KIDNEY TRANSPLANTATION: FIRST EXPERIENCE IN TURKEY

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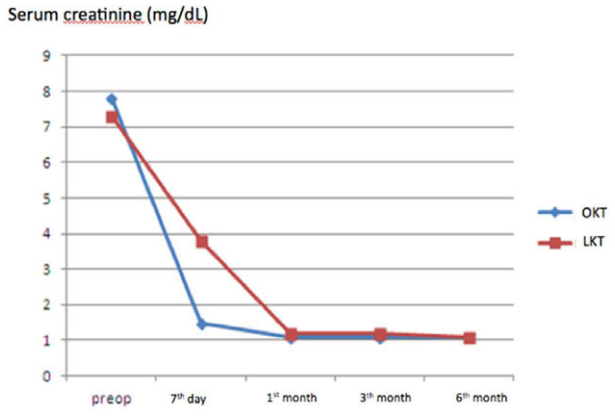
Background:
The aim of this study is to share our experience with laparoscopic kidney transplantation (LKT) from cadaveric donors.
Methods/Materials: Between November 2015 and July 2016, 7 patients (2 males, 5 females) received a cadaveric kidney by transperitoneal LKT in our clinic. Five contralateral kidneys obtained from the same cadaveric donors were transplanted with classical open method (OKT) into 5 patients (3 male, 2 female).
Results: There were no differences between the two groups in terms of age, gender, cold ischemia time, delayed graft function and acute rejection. The mean age of patients with LKT was 40.5 ± 12.2 (20–54) years. Mean cold ischemia time was 591.1 ± 220.5 (330–910) minutes, mean operative time was 215 ± 33.5 (190–280) minutes, mean arterial anastomosis time was 23.1 ± 5.8 (13–32) minutes, mean venous anastomosis time was 36.5 ± 6.6 (28–44) minutes and ureteroneocystostomy was 21.8 ± 3.4 (19–25) minutes. Acute cellular rejection developed in two patients. Mycotic pseudoaneurysm was diagnosed in two patients who underwent LKT and OKT from the same cadaveric donor. Also BK virus infection was developed in two other patients who had kidney transplantation from the same cadaveric donor. Patients with pseudoaneurysm had a graft nephrectomy on posttransplant third month. In the LKT group, mean postoperative 7th day creatinine level was 3.8 ± 2.5 mg / dl, whereas in the OKT group 1.5 ± 0.9 mg/dl, however this difference was not significant probably due to low number of samples. There was no difference in the mean creatinine values of posttransplant 30th day, 3rd and 6th months between the two groups (Image 1).
Conclusion: LKT should still not be considered as a standard modality for kidney transplantation; however, it can be performed in selected cases in experienced centers.



Clinical Kidney Donation and donor types

BOS193 EN BLOC RENAL TRANSPLANTATION: SURGICAL COMPLICATIONS AFTER 25 YEARS OF FOLLOW-UP

Maria Angeles Moreno De La Higuera, En Bloc Renal Transp, Natividad Calvo Romero, En Bloc Renal Transp, Isabel Perez Flores, En Bloc Renal Transp, Marta Calvo Arevalo, En Bloc Renal Transp, Amir Shabaka, En Bloc Renal Transp, Virginia Lopez De La Manzanara, En Bloc Renal Transp, Beatriz Rodriguez Cubillo, En Bloc Renal Transp, Angel Gomez Vegas, En Bloc Renal Transp, Jesus Blazquez Izquierdo, En Bloc Renal Transp, Ana Isabel Sanchez-Fructuoso, En Bloc Renal Transp
Hospital Clinico San Carlos, Spain

Introduction: En bloc pediatric transplantation (EBPT) began with the aim of increasing donor pool due to the existing high demand for donors. At its inception it was considered a type of suboptimal transplantation due to its association with a high incidence of vascular, urological and immunological complications. The main objective of this study was to update information on EBPT with the largest case series that exists on a worldwide scale.
Methods: In a retrospective study the results obtained from brain death donors (BDD) (n = 770) were compared to those of EBPT (n = 100) from January 1990 till December 2012. The variables collected for analysis: demographic factors (age and sex of recipients, age and weight of donors), renal function, graft survival, recipient survival, surgical complications: thrombosis, lymphocele, urological complications and renal artery stenosis and need for revascularization with angioplasty and/or stents. Subsequently in a second analysis, the association between the following variables was studied: graft survival, thrombosis, angioplasty, stents and appearance of lymphoceles with the different factors that were considered to be related in accordance with published literature and own experience.
Results: We analyzed 770 BDD renal transplants and 100 EBPT renal transplants. The median of follow-up was 12.8 years (IQR 8.1–17.2). The mean age of recipients from BDD was 49 ± 13.2 years, and that of recipients from EBPT was of 46.6 ± 13.4 years. Graft loss due to surgical complications was more frequent in EBPT than in BDD (15% vs. 2.2 % in BDD; $p < 0.001$) while interstitial fibrosis and tubular atrophy was more frequent in BDD (13% vs 2%; $p < 0.001$). A significant association between incidence of thrombosis and surgeon involved was observed ($p = 0.045$). There was no statistically significant association with donor age or weight, recipient age or use of heparin.
Conclusions: EBPT offers a good survival rate after overcoming the possible surgical complications that may arise.

Clinical Kidney Surgical technique

BOS194 RENAL TRANSPLANT IN RECIPIENTS WITH COMPLETE IVC THROMBOSIS

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Introduction: Thrombosis of the inferior vena cava (IVC) poses a unique challenge for renal transplant. Absence of adequate venous outflow for the transplant kidney makes transplant technically challenging and in most cases, impossible. There has been reports of successful kidney transplant with venous drainage to well developed collaterals, portal venous drainage and to suprarenal IVC. In this abstract we present four cases of renal transplant in recipients with complete IVC thrombosis.
Methods: Retrospective review of all transplants carried out between 2010 and 2016 was done, where the recipients were known to have complete IVC thrombosis. All the recipients were investigated extensively with mapping of possible venous drainage of potential transplant. Possible strategies for transplant were discussed and agreed in a multidisciplinary meeting involving transplant surgeons, nephrologists and vascular radiologists.
Results: Four renal transplants were carried out in the study period. Where the recipients were known to have complete infra renal IVC thrombosis. Mean recipient age was 30.5 years, all of whom were established on haemodialysis. Three of these recipients had positive thrombophilia screen (Table 1). A deceased donor transplant was planned in view of uncertainty in establishing a venous drainage and avoiding an 'orphan' living donor kidney. The details of the transplants are presented in table 1. Three transplants were successful, whereas one failed to establish adequate venous drainage and was removed soon after transplant. All the recipients were placed on long term anticoagulation.
Conclusions: Renal transplant is possible where the recipient has complete IVC thrombosis. A thorough investigation and venous mapping is critical to planning. A multidisciplinary discussion and agreed plan for transplant will help

Recipient Age	Sex	Cause of CKD	Thrombophilia Screen	Donor	Venous Drainage	Outcome
37	F	Diabetic Nephropathy	Factor V Leiden – Heterozygous	44/F/ DBD	Left ovarian vein	Successful
38	M	Renal Dysplasia	Factor V Leiden – Heterozygous + Antiphospholipid	30/M/DBD	Suprarenal IVC	Failed on table
30	M	Interstitial Nephritis	Lupus anticoagulant	48/M/ DBD	Right external iliac vein	Successful
17	M	Congenital Nephrotic Syndrome	None	46/M/ DBD	Left native renal vein	Successful

achieve a favourable outcome. Role of lifelong anticoagulation seems justifiable, although evidence is lacking in this area.

Basic Heart Surgical technique

BOS196 ABOUT THE USE OF FOETAL HEART IMPLANTS FOR HEART LESION REPAIR IN RATS

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[1]Ulb Laboratory of Experimental Medicine, Belgium; [2]Ipg, Belgium

Background: The new tendency in heart reparative surgery consists in reengineering new myocardium through stem cells culture in vitro with subsequent implantation on the altered heart. Results are controversial though promising. On the base of foetal organ implantation as a "culture in vivo", we have tried to shunt the in vitro procedure and to implant directly foetal heart, i.e. precursor cells on the surface of a cauterisation lesion of the heart apex in Rats.
Methods: Recipients were 30 Wistar male rats 4–8 months aged. Donors were Wistar foetuses aged 14–19 days in utero development. During the same operative action a lesion of 8x7x2 mm was formed by thermocautery (T T & R, 2015, 5, 2) and the implant was placed under a 9x9x1 mm chitosan membrane fixed to the healthy myocardium by 8° stitches. The follow up included ECG, cardio echography and histology at 10, 30, further monthly up to 10 months. As control 8 intact rats, 20 rats with only heart lesion, 20 rats with lesion covered by a chitosan membrane were used. (Ethic Committee agreement N°508)
Results: The surgery survival was about 95% when all the technical details were resolved. Functional recovering was the best after foetal heart implantation. Some improving was also noted after covering the lesion with chitosan, in comparison with control with only heart lesion. Morphologically, coagulation necrosis, oedema, inflammatory reaction was observed in the early delays, which turned to fibrosis in the late ones. Chitosan has caused a significant inflammatory reaction and its degradation was practically complete after 4 months. The implant first regressed, then re-differentiated or simply developed in tight contact with the host myocardium. It is difficult to establish whether implanted cardio myoblasts have penetrated the host myocardium or not.
Conclusion: The implantation of foetal heart under a chitosan cover seems to play an important role in the heart functional recovery after severe apical lesion in the rat.

Clinical Heart Biomarkers and molecular changes

BOS197 BIOMARKERS' PANELS INCLUDING ST2: DIAGNOSTIC EFFICACY IN PATIENTS WITH REJECTION IN THE LONG TIME AFTER HEART TRANSPLANTATION

Sergey Gautier, Alexey Shevchenko, Natalia Mozheiko, Olga Gichkun, Alexandra Aksenova, Kate Stakhanova, Elena Nikitina, Kseniya Bolshakova, Olga Shevchenko

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Background: One of the causes of graft dysfunction and its loss after heart transplantation (HTx) is rejection. Different studies demonstrated participation of a number of biomarkers in the development of rejection, as well as the possibility of using the biomarkers' data to predict and to stratify risk of heart transplant rejection. Using a panel of several analytes increases the sensitivity and specificity of multimarker tests.
Methods: We studied 144 recipients (111 men; 44 ± 14 years) from 3 to 1559 days after HTx. The concentration of soluble CD40 ligand (sCD40L), vascular endothelial growth factor (VEGF-A), platelet-derived growth factor (PDGF-BB) were measured using multiplex immunoassay (xMAP technology). The concentrations of ST2 were measured by ELISA. Biomarkers' levels were measured in peripheral blood plasma taken at the same day as the endomyocardial biopsy (EMB).
Results: The ST2 level was significantly higher in patients with heart rejection (n = 12) in the long time after HTx (p = 0.01). The sCD40L, VEGF-A and PDGF-BB concentrations didn't show significant differences between pts with rejection and without it in the long time after HTx (p = 0.9, p = 0.7, p = 0.07 respectively). The relative risk of heart rejection was significantly higher in pts with high ST2 level (above the median value) (RR=2.6 ± 0.33; 95% CI [1.37–4.91]). Combinations with other biomarkers increased the risk of development of rejection (figure 1).

The highest diagnostic efficacy for heart rejection can be reached by a panel of two biomarkers: ST2 and PDGF-BB (RR = 5.0 ± 0.56; 95% CI [1.68–14.92]).
Conclusion: Measurement of ST2 level in combination with other biomarkers has diagnostic efficacy in patients with rejection in the long time after HTx.

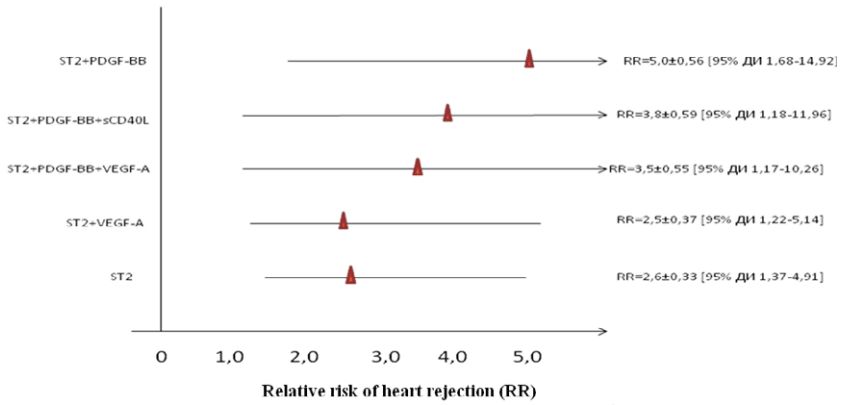

Figure 1. The relative risk of heart rejection in the long time (> 1 year) after HTx in pts with a biomarkers concentration exceeding the median value

BOS198 PLASMA ST2 LEVEL BEFORE AND AFTER HEART TRANSPLANTATION

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Background: The rejection is one of the most serious complications affecting the prognosis in heart transplant recipients. The development of biomarkers data for graft rejection detection allows to improve early diagnostic and increases the life span of patients by minimizing post-transplant complications. ST2 is the marker used primarily for predicting the risk of heart failure. We measured ST2 level to assess the risk of rejection development.
Methods: The study included 98 pts (78 men; 43 ± 14 years) with terminal stage of heart failure, before and during 4 years after heart transplantation (HTx) and healthy individuals (20 men, 38 ± 9 years). Acute cellular and humoral rejection was identified by endomyocardial biopsy (EMB). Tacrolimus, corticosteroids and mycophenolate mofetil were included in immunosuppressive therapy after HTx. The concentrations of ST2 were measured by ELISA.
Results: In the pts pretransplant plasma level of ST2 was 74.4 [40.3; 124.7] ng/ml and it was significantly higher than in healthy individuals (12.2 [6.0; 20.8] ng/ml, p = 0.00). After HTx ST2 level decreased significantly (p = 0.01). During the follow up the rejection was diagnosed in 37 pts. The ST2 level in recipients with rejection was 42.3 [30.5; 79.7] ng/ml, and was higher compared with recipients without it (34.7 [22.4; 62.1] ng/ml; p = 0.03). The ST2 level was significantly higher in pts with heart rejection a year after HTx (p = 0.01), but didn't show difference in pts with rejection and without it in the first month and first year after HTx.
Conclusion: Plasma ST2 level decreases after HTx. The ST2 level is higher in pts with heart rejection than in pts without it a year after HTx.

Translational Heart Rejection

BOS199 CLINICAL AND HEMODYNAMIC PHENOTYPES OF GRAFT DYSFUNCTION: IMPROVING ETIOLOGICAL DIAGNOSIS BY BIOPSY MOLECULAR PROFILING

Laura Borgese[1], Agnese Gaudenzi[1], Valentina Agostini[1], Jeff Reeve[2], Marco Masetti[1], Barbara Corti[1], Francesco Grigioni[1], Ornella Leone[1], Philip Halloran[2], Luciano Potena[1]
[1]Bologna University Hospital, Italy; [2]University of Alberta, Edmonton, Canada

Introduction: Pathology grading of endomyocardial biopsies (EMB) still remain the reference standard for the diagnosis of T-cell-mediated (TCMR) and antibody-mediated (ABMR) rejections in heart transplant (HT). However, EMB findings are often unrelated to clinical and hemodynamic presentation. To improve diagnostic accuracy of EMB, we analyzed tissue molecular transcripts by the Molecular Microscope Diagnostic System (MMDx), comparing molecular (Mol-Rej) and pathological (Path-Rej) diagnosed rejections to graft function.
Methods: We analyzed seventy-four EMBs from 47 patients at a median of 9 months (range 1 week-20y) after HT. Specimens were graded according with standard pathology criteria and by MMDx system. Patients also underwent right heart catheterization and cardiac ultrasound.
Results: 23 (33%) EMBs showed molecular classifiers indicative of rejection (12 ABMR, 3 mixed and 8 TCMR). As compared with EMBs with normal molecular profile, Mol-Rej was associated with lower ejection fraction (53 ± 2 vs 64 ± 1% P < 0.01), higher right atrial pressure (9.1 ± 0.9 vs 5.9 ± 0.5, P < 0.01) and higher proportion NYHA class III (24 vs 38%; P = 0.09). Path-Rej was found in 32 (43%) EMBs. Clinical and hemodynamic phenotypes did not differ between Path-Rej and EMBs with normal pathology grading. EMBs graded as completely negative showed 80% concordance rate with normal molecular profiling, while Path-Rej showed only 40% concordance rate with Mol-Rej.
Conclusion: Molecular diagnosis of rejection by the MMDx system was consistently associated with graft dysfunction phenotypes. On the other hand, pathological classification did not correlate with graft function phenotypes, suggesting that a molecular-based approach may improve the etiological classification of rejection, and help to illuminate the grey areas of EMB pathological rejection grading.

Basic Heart Biomarkers and molecular changes

BOS200 IMMUNE MONITORING OF REGULATORY CD4 CELLS IN HEART RECIPIENTS UNDER IMMUNOTHERAPEUTIC INDUCTION: ONE-SINGLE DOSE VERSUS TWO-DOSE BASILIXIMAB

Sandra Garcia[1], Elizabeth Sarmiento[1], Leticia Calahorra[1], Antonio Gallego[1], Eduardo Zatarain[1], Paula Navas[1], Iago Sousa-Casasnovas[1], Raquel Lerma[1], Javier Carbone[2]
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Background: The impact and indication of induction immunosuppressive therapy 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 selected cases. Immune monitoring of regulatory CD4 cells can provide useful information in this regard.
Methods: A comparative analysis between the use of the recommended two doses of 20 mg (2D, n = 18) of anti-IL2R-alpha monoclonal antibodies (Basiliximab) versus a single dose (1D, n = 32) in selected patients of a single center was performed. We analysed regulatory CD4 cell kinetics during the first 6 months after transplantation. Assessment points: pre-HT, day [d] 7, d15, d30, d60, d90, d180. Maintenance immunosuppression included steroids, tacrolimus and mycophenolate mofetil. Percentages and total counts of distinct lymphocyte subsets were studied by flow-cytometry.
Results: In patients using 2 doses of Basiliximab, a decrease of CD4 + CD25 + CD127low regulatory cells was observed as compared with pre-transplant values between day 7 and 60; while in patients that received a single dose the percentage remained stable. Baseline (pre-transplant percentages were similar in both groups (5.45 ± 2.48 vs 5.36 ± 3.31%, p = 0.93). Lower levels of regulatory CD4 + cells were observed up to day 30 in patients using 2-doses: day 7 2.52 ± 2.62 vs 4.76 ± 3.90%, p = 0.046; day 14 2.75 ± 2.55 vs 5.08 ± 5.17%, p = 0.074 and day 30 2.96 ± 2.69 vs 5.61 ± 3.78%, p = 0.014.
Conclusion: In a 6 month post transplant immune monitoring follow-up study of a single cohort, one-dose of Basiliximab maintained higher levels of regulatory CD4 + cells compared to a conventional 2-dose regimen. This information is of interest since CD4 regulatory cells are considered to have an important role in allograft rejection.

Clinical Heart Immunosuppressive agents

BOS201 EFFICACY AND SAFETY OF DIFFERENT IMMUNOSUPPRESSION STRATEGIES (IS) IN COMBINED HEART AND KIDNEY TRANSPLANTATION (CHKT)

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Background: Graft survival within 5 years after kidney transplantation (KT) is now achieved in > 95% of recipients, but chronic graft deterioration remains as a limiting factor of long term survival. Due to heart transplant (HT) extended survival, post-transplant renal failure has become a major factor impairing quality of life with significant prognostic implications. One of the main reasons may be the toxicities associated with calcineurin inhibitors (CNI). CNI minimization protocols in trials that analyze isolated KT or HT are safe regarding rejection and allograft dysfunction. There are no data about the maintenance IS in cHKT.
Methods: We analyzed 22 consecutives cHKT performed at the Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina between 01/2006–09/2016. 3 patients (p) were excluded because they died at early post-transplantation. The initial IS was triple therapy consisting of tacrolimus (CNI with serum levels around 10 ng/ml), mycophenolic acid (MA) and corticosteroids (CS). During the follow up the cohort was divided per IS into two groups: Group 1: standard group, including patients who continued with initial IS; Group 2: CNI withdrawal/sparing group (serum levels < 5 ng/ml). Causes for switch IS: nephrotoxicity, infection for BK virus, tolerance, digestive intolerance, vascular allograft disease and cancer.

Results

	Group 1 (N: 10)	Group 2 (N: 9)
Rejection		
Cellular	2p	1p
Antibody mediated	1p	0p
Severe Infections	6p	0p
Tumors	1p	2p
Ejection Fraction	>60%	>60%
Mortality		
Total	30%	22%
Sepsis	100%	0%
Tumors	0%	100%

The subgroup minimized by nephrotoxicity or BK nephropathy showed an increase in the Creatinine Clearance of 22 ml/min at 6 months of the switch.
Conclusion: This study suggests that conversion to mTOR-inhibitor based IS with CNI minimization or elimination as a treatment strategy is effective and safe in cHKT recipients.

The standard group showed a clear trend towards a higher infection rate and sepsis mortality, with no difference in grafts rejection rate or grafts function.

IS with low-dose tacrolimus resulted in improved renal function without immunological risk.

Clinical Heart Rejection

BOS202 RECURRENT ANTIBODY-MEDIATED REJECTIONS EPISODES MIGHT PROMOTE THE DEVELOPMENT OF RAPIDLY PROGRESSIVE FORM OF CARDIAC ALLOGRAFT VASCULOPATHY

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Background: Cardiac allograft vasculopathy (CAV) is an important cause of graft loss after heart transplantation. Humoral side of rejection is more and more described as an important risk factor for CAV.

	Stable CAV (n = 11)	CAV progression n = 4	p
Recipient characteristics			
Age (years)	30 (24–50)	40 (33–43)	0.896
Hypertension	8 (73)	3 (75)	1
LDLc at 1 year (g/L)	1.1 (1–1.3)	1 (0.9–1.1)	0.395
Diabetes mellitus	3 (27)	1 (25)	1
Donor characteristics			
Age	37 (23–49)	39 (29–46)	0.896
Female gender	2 (18)	0	1
Transplantation			
Ischemic time (min)	199 (158–230)	230 (212–234)	0.47
Positive IgG CXM	0	0	1
AMR			
HTX-AMR interval (months)	40.7 (37–55)	35 (15–62)	0.79
LVEF	60 (47–65)	62 (50–69)	0.65
MFI of ID DSA	7,383 (3,410–11,843)	8,828 (7,580–10,257)	0.6
Cumulative MFI	10,914 (4,803–16,333)	25,733 (16,330–3,4090)	0.12
DSA with MFI > 3000	8 (73)	4 (100)	0.52
ID DSA class II	11 (100)	3 (75)	0.27
De-novo ID DSA	11 (100)	2 (50)	0.52
AMR recurrences (%)	1 (9)	3 (75)	0.03

Methods: We performed a retrospective, single center, observational study. We included all consecutive patients with (1) definite diagnosis of antibody-mediated (AMR) rejection treated at our center, (2) pre and post AMR coronary angiography available, (3) without history of severe CAV requiring angioplasty. We compared pre and post-AMR coronary angiograms to analyze the influence of AMR on CAV development. Characteristics of progressors were compared to non-progressor to determine risk factors for CAV development. Prognosis was evaluated by the composite endpoint of death and chronic cardiac allograft dysfunction.
Results: One hundred and three patients have been treated for AMR at our institution. Finally, 15 patients were included. Median interval between heart transplantation and AMR was 3 years. AMR was mostly due to high titer de novo class II DSA. CAV appeared or worsened after AMR in four patients. Recurrences of AMR were significantly more common in patients with CAV progression whereas other risk factors of CAV were well balanced between groups (see table). Composite endpoint of death and chronic cardiac allograft dysfunction occurred more often in progressive CAV patients compared to stable CAV patients (n = 3/4 compared to 2/11, log rank test: p = 0.02).
Conclusion: AMR can promote rapidly progressive forms of CAV. Recurrent AMR might be an important trigger of CAV progression. Progressive CAV after AMR is associated with poor outcomes.

Translational Heart Immunology

BOS203 INTRAVENOUS IMMUNOGLOBULIN THERAPY INCREASES SERUM ANTI CLOSTRIDIUM DIFFICILE TOXIN SPECIFIC ANTIBODIES IN HEART TRANSPLANT PATIENTS

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Background: New therapeutic approaches to improve survival in patients with severe infections after solid organ transplantation (SOT) are needed. We have previously addressed that intravenous immunoglobulin (IVIG) might be an adjunctive therapy leading to an increase in specific anti cytomegalovirus (CMV) antibodies. *Clostridium difficile* (CD) infection is a common opportunistic infection in SOT. This is the first time that passive transfer of anti CD toxins is addressed in serum of patients after non specific IVIG therapy.
Methods: 19 SOT patients (heart n = 13, kidney n = 4, liver n = 2) presenting severe infections and hypogammaglobulinemia (IgG<600 mg/dL) were included in an ongoing randomized multicenter clinical trial. Patients received either IVIG (n = 9) additionally to conventional antimicrobial treatment vs conventional therapy alone (n = 10). IVIG therapy included 5 doses of IVIG (2 doses of 15 grams (g) [7 to 15 days after infection diagnosis] followed by 3 doses of 20 g). We tested serum IgG and specific antibodies (anti-*CD* antibodies against toxin A [anti-CDTA] and toxin B [anti-CDTB], anti-CMV among other specific antibodies, in a single center sub-study by commercial ELISA before visit 1 and at the last visit, 30 days after last dose.
Results: No significant differences between groups in the baseline levels were found. IVIG was associated with significant higher levels in serum IgG anti-CDTA, anti-CDTB and anti-CMV. Comparison by T test of values obtained after treatment vs values at visit 1 showed significantly higher levels in the IVIG group: Anti-CMV 44398 ± 12564 vs 17518 ± 9707 units, $p < 0.001$; anti-CDTB 0.26 ± 0.08 vs. 0.10 ± 0.036 optical density units (OD), $p < 0.001$; anti-CDTA 0.19 ± 0.05 vs. 0.08 ± 0.03 OD, $p < 0.001$.
Conclusion: We demonstrate utility of IVIG for the passive transfer of anti CD toxins A and B and confirm previous observations for anti CMV antibodies. Funds from FIS Project 1501472 and from EudraCT 2012-001327-12 with participation of FEDER funds.

Clinical Heart Cardiovascular complications

BOS204 ATRIAL FLUTTER AFTER CARDIAC TRANSPLANTATION: ELECTROPHYSIOLOGIC CHARACTERIZATION AND CATHETER ABLATION

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Purpose: Cardiac transplantation (CTX) is an effective treatment for end-stage heart disease. Atrial flutter (AFL) and atrial tachycardia are the most frequent supraventricular arrhythmias in this clinical setting and are associated with significant morbidity and mortality. They have been related to acute rejection (AR) and graft vasculopathy and their management is challenging.

Radiofrequency catheter ablation (ABL) is the treatment of choice in AFL. However, there are few reports in the literature about its effectiveness in patients (ptes) following CTX.

The purpose of this study is to describe the clinical and electrophysiologic characteristics of AFL occurring late after CTX and to evaluate the role of ABL.
Methods: CTX recipients with AFL referred for ABL were included. Activation and entrainment mapping were utilized to define AFL circuit and guide the ablation under fluoroscopic navigation. An endomyocardial biopsy was done to rule-out AR.
Results: 5 CTX recipients (3 male and two female; 26–63 years old) with AFL were included. The atrio-atrial anastomoses technique was done in all of them. Time from CTX to ABL was 4–15 years. There were no cases of AR.

Typical cavotricuspid isthmus (CTI) dependent AFL in donor atrium was confirmed in all ptes with a counterclockwise circuit in four of them and a clockwise circuit in one pte. Recipient right atrium was in sinus rhythm, dissociated from donor atrium in 4 ptes, consistent with bidirectional block in the suture line. One pte had recipient right atrium with atrial AFL. ABL of CTI resulted in AFL termination in all the ptes, without procedure-related complications. "Electric" isthmus was smaller than in native hearts, which contribute to a shorter procedure time. There was no arrhythmia recurrence during follow-up.
Conclusion: AFL after CTX had similar characteristics than in native hearts and was not associated with AR. ABL was safe and effective in these ptes.

Clinical Heart Immunosuppressive agents

BOS205 DEVELOPMENT OF RENAL FUNCTION IN PATIENTS RECEIVING SIROLIMUS WITH REDUCED CNI-DOSAGE AND WITHOUT CNI-MEDICATION

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Objectives: It is currently not known whether the sirolimus in combination with calcineurin inhibitors (under dosage reduction) is superior to the calcineurin inhibitor free therapy (mTOR-inhibitors ± MMF ± prednisolone).
Methods: We compared 2-year clinical outcomes in 25 patients receiving CNI free immunosuppressive therapy with sirolimus ± MMF/ ± prednisolone from 2002 to 2013 (CNIF-group) with 25 patients receiving sirolimus or sirolimus combined with cyclosporine or tacrolimus from 2002 to 2013 (CNI-group). The primary endpoint was development of the renal function between the two groups.
Results: Groups were comparable regarding baseline characteristics such as age, primary diagnosis, body mass index (BMI), creatinine values and GFR. Compared to the CNI group, kidney function improved in the CNIF group over time ($p < 0.05$). Glomerular filtration rate improved from 33.1 ml/min at baseline to 53.9 ml/min after 24 months in the CNIF group and decreased from 38.5 ml/min to 38.1 ml/min in the CNI – group ($p < 0.05$). Creatinine value decreased from 2.3 mg/dl at baseline to 1.8 mg/dl after 24 months in the CNIF – group and increased from 2.3 mg/dl to 2.8 mg/dl in the CNI – group ($p < 0.05$). Three-year survival did not differ significantly between the groups ($p > 0.05$). Laboratory parameters such as liver values, cholesterol values, triglycerides and blood count (erythrocytes, thrombocytes, leucocytes) did not differ significantly between the groups during two year follow up ($p > 0.05$).
Conclusions: CNI – free therapy with sirolimus had beneficial effects on kidney function in HTX patients with chronic renal failure compared to patient with reduced CNI – dosage. Secondary endpoints such as survival and laboratory parameters did not differ significantly between the groups. We conclude that CNI free therapy with everolimus could be an option in patients with progressive renal failure, due to CNI – nephrotoxicity.

BOS206 DOES EVEROLIMUS IMPACT LONG TERM CLINICAL EVENTS IN HEART TRANSPLANTATION?

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Introduction: Prospective randomized trials (RTs) compare everolimus (EVE) and mycophenolate (MMF) in de novo heart transplantation (HT); however, long term data on clinical endpoints are lacking.

Methods/Materials: We reviewed 5 years post-transplant follow-up of all patients (pts) who had been enrolled in RTs about EVE de novo in our Center. We analyzed occurrence of fatal and non fatal major cardiovascular events (MACE), all-cause mortality, cancers, and renal function. Given the frequent cross-over during the follow-up, we performed both an intention-to-treat (ITT) and an on-treatment (OT) analysis, defined post-hoc as the drug taken for most of the time.
Results: 93 pts (80% males, 53 ± 11 years, HT 2005-14, glomerular filtration rate (GFR) 70 ± 32 ml/min) were enrolled: 57 randomized to EVE, 36 to MMF, without statistically significant differences at baseline. 32 (34%) pts had at least one cross over, 11 (12%) for clinical reasons (cancers, renal failure, rejection), 21 (23%) for intolerance. Tolerability was lower in EVE arm ($p = 0.03$), mostly due to pericardial effusions, but comparable to MMF after 3 months from HT ($p = 0.53$). ITT analysis showed no differences on any study endpoint between MMF and EVE (all $p > 0.5$). Among 19 fatal and non fatal MACE, 5 occurred during EVE treatment. OT analysis showed in EVE group a significantly lower incidence of fatal and non fatal MACE (7.6 ± 4.2% vs. 33.3 ± 7.1%, $p < 0.01$) at 5 years, whereas mortality (9.6 ± 4.5% vs. 10.5 ± 4.4%), cancer incidence and change in renal function were similar (all $p > 0.5$).
Conclusion: This is a post-hoc analysis of pts randomized in trials with different endpoints. We found suggestive evidence of potential benefits of EVE in reducing long-term MACE, without affecting survival. These data are only hypothesis generating, but they suggest a delayed introduction of EVE to favor tolerability, aiming to take better advantage of its possible benefits.

Clinical Artificial Organ Other

BOS207 A RARE CASE OF RESPIRATORY FAILURE IN A BOY FOLLOWING VENTRICULAR ASSIST DEVICE INSERTION. CASE REPORT

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Introduction: Ventricular Assist Device (VAD) is a bridging therapy in patients waiting for a heart transplant. We report a VAD implanted 6 year old boy who developed respiratory failure following surgery.
Case Presentation: A 6 year old boy undergone pulmonary banding for transposition of great arteries following birth. Senning atrial switch and VSD repair was performed 3 years later. At 6 years of age, tricuspid annuloplasty was performed. Following impaired hemodynamics postoperatively he was transferred to our center for an urgent heart transplantation. Bridging therapy with a Heartware VAD implanted. He was extubated at 48th hour postoperatively but reintubated due to difficulty in breathing and desaturation. Transesophageal echocardiography without additional findings was followed by a bronchoscopy and revealed a narrowed left main bronchus which was considered to be due to the compression of the heart. Bronchial stent insertion did not give the chance of extubation. Decreased compliance was considered to be the cause of respiratory failure and tracheostomy was performed. He was weaned off ventilator after 1 month and transferred to ward with tracheostomy cannula in place and then decannulated. Four days following decannulation the patient discharged home. The boy rehospitalized for coughing and progressed atelectasis in lower zones of the left lung. Tips of the stent obscured in CT due to developed granulation tissue, could be seen by bronchoscopy. Left main bronchus was obstructed again by anterior compression following the removal of this stent. A biodegradable stent was then inserted and the boy was discharged home.
Discussion and Conclusion: VAD is a bridging therapy for a heart transplantation which may be required due to right heart failure following surgery of congenital heart defects. Respiratory failure is a frequent perioperative problem and may not primarily be a result of heart defects but pulmonary anatomic structure.

Clinical Heart Cardiovascular complications

BOS208 CLINICAL PHENOTYPES OF CARDIAC GRAFT DYSFUNCTION: LINGERING HEART FAILURE AND MULTIPLE ETIOLOGIES

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Background: Despite its clinical relevance, there is a lack of consensus regarding the definition of graft dysfunction (GD) in heart transplant (HT). Herein we aim to characterize clinical phenotypes of patients with GD, either acute or chronic, comparing their outcomes with stable patients. In addition, we explored the risk factors for outcome in GD patients.
Methods: We prospectively enrolled patients in two groups: stable de novo or long-term survivors and patients with GD. GD was defined as at least one of the following: ejection fraction (EF) <55%, symptomatic cardiac allograft vasculopathy (CAV), or new onset symptoms of heart failure. Study Endpoints were: combined and separate incidences of overall mortality and hospitalizations for cardiovascular events (CVE).

Results: We enrolled 134 consecutive HT patients. Patients with GD 32 (24%) had significant higher prevalence of class NYHA >II, low EF, CAV, and donor specific antibodies (DSA) (all $p < 0.05$), as compared with stable ones. Clinical presentation was highly heterogeneous: 6 (19%) had acute presentation, 3 for acute rejection, and 3 for acute coronary syndromes; 21 (66%) had chronic presentation: 17 (53%) associated with CAV, and 4 (13%) as chronic dysfunction after antibody-mediated rejection. 5 patients had acute symptoms but no-graft related cause emerged. During the 2 years follow-up, GD patients showed higher mortality (23 vs. 14%; $p = 0.01$) and higher CVE hospitalization rate (54 vs. 5%; $p < 0.01$) than the stable ones. Low EF, time from HT, and chronic clinical presentation ($p < 0.05$) were risk factors for the combined endpoint.
Conclusions: GD after HT is characterized by highly variable clinical presentation and is correlated with a particularly poor prognosis. CAV is the most frequent etiology, and DSA are more often found in patients with GD than in stable ones, but do not seem to influence outcome.

Clinical Heart Surgical technique

BOS209 CASE REPORT: THE WORLD'S FIRST HEART-KIDNEY TRANSPLANT FROM DONATION AFTER CIRCULATORY DETERMINED DEATH

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There is an increasing demand for donor organs for patients with both end-stage heart failure and renal disease. Kidney donation after circulatory determined death (DCD) has been well established and more recently, DCD donation has increased donor organ utilisation in cardiac transplantation in the UK. We report on the first case of a combined DCD heart-kidney transplant with distant procurement.
Case report: MS, 52 year old, B positive male with a diagnosis of non-ischaemic cardiomyopathy possibly due to left ventricular non-compaction and concurrent end-stage renal failure due to focal segmental glomerulosclerosis underwent a combined heart-kidney transplant in April 2016. At the time of transplant, MS had been waiting 404 days for donor organs. The donor was a 49 year old female who suffered catastrophic intracerebral haemorrhage and consented for DCD organ retrieval.

The heart was retrieved and perfused ex-situ with donor blood during transportation (Organ Care System, TransMedics). The kidneys were flushed and put into cold storage for preservation during transport.

After assessment of the donor organs, the recipient was placed on to cardio-pulmonary bypass and an orthotopic heart transplant was performed via a median sternotomy. Following successful weaning of bypass, heparin was reversed and the chest closed. A heterotopic kidney transplant was then performed with the cardiac team on standby.

Post-operatively, the patient displayed good cardiac function with an initial cardiac index of 3 l/min/m2 and was extubated on the first post-operative day. The renal allograft displayed some primary graft dysfunction and required haemofiltration prolonging the requirement for intensive care. To date, there has been no evidence of allograft rejection and cardiac MRI confirms good bi-ventricular cardiac function with satisfactory renal function. This is the first reported case of a DCD heart-kidney transplant using this technique.

Clinical Liver Donation and donor types

BOS210 THE USE OF OCTOGENARIAN DONORS FOR LIVER TRANSPLANT

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Introduction: In the period 1/1/2015–31/1/2015 in Italy on 2360 patients in waiting list for liver transplant (LT), the waiting list drop out was 9.3% with a mortality of 5.3%. In light of the donor organ shortage and the high number of liver transplantation (LT) candidates on the waiting list several strategies have been introduced to increased the pool of donors. Among the criteria defining extended criteria donors (ECD), donor age is stretched most, so that the use of septuagenarian, octogenarian and even nonagenarian donors increasingly became common practice.
Method: A retrospective analysis of donors used in the period January 2012–June 2016 has been conducted in our institution. For our analysis we compared the outcome of recipients receiving donors with age ≥80 years vs. a matched cohort of donors with age <80. Donor demographics data (age, gender, cause of death, DRI, ICU stay, drug support), intraoperative data (CIT, WIT) and recipients characteristics (age, gender, MELD, etiology, portal vein thrombosis, post-transplant complications) were collected.
Results: A total of 40 old grafts (≥80 years) were used; there were no differences in incidence of PNF, PDF, re-transplant, or perioperative deaths between the 2 groups. Also complication rate (Clavien-Dindo >2) was similar.
Conclusion: Survival outcome with octogenarian donors resulted similar to that of matched group of recipients with donors <80 years; overall morbidity resulted not significantly increased. Ancient donors are safe and its use will be increase in the future. A policy of donor-recipient matching is crucial to obtain optimal results.

BOS211 "NON TOUCH" VENA CAVA TECHNIQUE AS AN IMPROVEMENT IN COMBINED LUNG AND ABDOMINAL ORGANS PROCUREMENT IN DONATION AFTER CIRCULATORY DEATH (DCD) MAASTRICHT III

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Background: Number of grafts from donation after circulatory death (DCD) has been increasing in the last years. Functional superiority of DCD organs are suggested when lungs are perfused with cold/room temperature perfusion and livers with normothermic regional perfusion (NRP). Thus, an accurate surgical technique is needed to combine thoracic and abdominal organ procurement. We describe the technique used in our centre based on not clamping the thoracic vena cava (VC).
Methods: Withdrawal of life support and death confirmation according to Spanish law takes place in the operating room. After rapid laparotomy and thoracotomy, both suprailiac aorta (Ao) and inferior VC are cannulated. Descending thoracic Ao is cross-clamped. As a variation of previously described techniques, the thoracic VC (inferior VC nor superior VC) is not initially clamped in order to ensure an adequate blood volume return to the NRP circuit which is crucial for a good perfusion of abdominal organs. Pulmonary artery is cannulated to flush lungs and left atrial appendage is opened for drainage. Liver function is monitored every 30 min (AST, ALT, pH, lactates, hematocrit). After 120 min, NRP perfusion is stopped and abdominal organs are flushed with cold Wisconsin preservation solution and removed as in a standard deceased donor.
Results: In 2016, 3 livers, 6 lungs and 6 kidneys were used for transplantation (12 recipients) using this technique in our center. In all 3 donors, pump flow was 1.7–2 l/min and extra volume was added to the circuit. Timings for NRP are described (Table 1). All allograft presented an excellent immediate function and 11 of 12 patients were discharged from hospital after transplantation. The remaining admitted patient has a good lung graft function 7 months after transplant.
Conclusion: Combined procurement of lungs after room temperature perfusion and liver and kidneys after NRP without initial clamping of the thoracic VC is feasible with excellent graft function after transplantation.

Withdrawal to asystole*	Functional warm ischemia*	Cannulation time*
16	18	11
16	18	7
13	19	9
*min		

BOS212 ANALYSIS OF REJECTED LIVER ALLOGRAFTS IN FINLAND – THE ROLE OF GLUTAMYLTRANSFERASE AS A PREDICTOR OF GRAFT STEATOSIS

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Background: Liver-transplantation activity is limited by the shortage of suitable grafts. Donor-liver macrovesicular steatosis (MaS), but not microvesicular steatosis (MiS), predisposes to ischemia-reperfusion injury and is associated with reduced graft survival. The increasing population prevalence

of fatty-liver disease underlines the importance of identifying MaS in potential donor livers.

We analyzed the liver grafts rejected for transplantation in Finland between Feb 2014 and Dec 2016, and particularly the role of glutamyltransferase (GT) in predicting graft steatosis.

Materials and Methods: 159 rejected cadaveric-donor liver grafts were studied. Donor selection was based on the age, medical history, laboratory values, body-mass index, optional liver ultrasound before the organ retrieval, and macroscopic graft inspection. Rejected grafts were biopsied at the organ procurement (148 biopsies available).

Results: The most common reasons for rejecting the graft were abnormal liver functional tests, with ultrasound verified hepatic steatosis and history of alcohol abuse.

GT correlated moderately with MaS ($r = 0.52$, $p < 0.001$), but poorly with MiS ($r = 0.36$, $p < 0.001$). Improved correlation between GT and MaS was observed among alcohol-abusers ($r = 0.67$, $p < 0.001$).

Area under the curve (AUC) for GT in predicting >30% MaS was 0.77 (95% CI 0.68–0.87), and >60% steatosis, 0.79 (95% CI 0.69–0.90). The optimal GT-cutoff for detecting >30% and >60% MaS were, respectively, 66 U/l (sensitivity 76%, specificity 68%) and 142 U/l (sensitivity 66%, specificity 83%). Among alcohol-abusers, a GT value >90 U/l showed 100% sensitivity for >60% MaS. AUC for GT in predicting liver fibrosis stage 2–4 was 0.82 (95% CI 0.71–0.92, $p < 0.001$, optimal cutoff 68, sensitivity 92%, specificity 61%).

Conclusions: Abnormal liver values, steatosis and alcohol abuse were the main reasons for rejecting liver-graft offers in Finland. GT proved useful in predicting moderate and severe liver graft macrovesicular steatosis.

Clinical Liver Allocation

BOS213 SPLIT-LIVER PROGRAM, THE NEW ALLOCATION SYSTEM IN ITALY: THE RESULTS OF FIRST YEAR ACTIVITY

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Background: The *split-liver* (S-L) transplant program allows two transplants from the same graft, on pediatric and on adult recipient. Since 25.08. 2015 the S-L allocative system has been modified to improve organ availability for the pediatric liver *waiting list* (WL). So far, we assess whether the new national program has been effective.

Methods: Each donor, aged ≤50 years, on standard risk, in the absence of super-urgent (UNOS Status 1) and urgent cases (MELD score ≥ 30), has been primarily offered to all pediatric transplant centers so they could directly evaluated the feasibility of the S-L technique, regardless of any graft evaluation by procurement center. The pediatric donor age has been raised from 15 to 18 years.

Results: From 25.08.2014 to 24.08.2015, 75 livers have been offered to pediatric liver transplant centers according to the old protocol criteria. 35 (46.7%) grafts accepted and 28 (80%) subjected to S-L technique with 56 left and right S-L transplanted. From 25.08.2015 to 24.08.2016, we recorded 252 liver offers according to the new criteria. In 70 cases (27.8%) there was acceptance of pediatric transplant center and so 51 livers (71.4%) were subjected to S-L technique with 101 left and right split-livers performed. The analysis of the new allocation system impact on pediatric WL shows a relevant increase of pediatric liver transplants (57.4%); we also registered an important increase of S-L pediatric transplants (81.2%). Unless the number of new listing pediatric patients has been increasing in the second period (36.5%), the mean waiting time for a pediatric liver transplant has not been changed (about 3 months).

Conclusion: By comparing the two periods, it is clear that the new allocation system resulted in an increase of 236% of liver offered as well as 100% of graft acceptance for S-L program. The most important result we registered, it was an increase of 80.6% of transplant performed by S-L technique and and increase of 81.2% of the pediatric ones.

Clinical Others Donation and donor types

BOS214 CHANGING PARADIGM: DONORS AFTER SUCCESSFUL TREATMENT OF HEPATITIS C VIRUS (HCV) INFECTION CAN BE A NEW SAFE DONOR SOURCE FOR NEGATIVE HCV RECIPIENT

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The new treatments for hepatitis C virus (HCV) infection have been shown to be highly effective in permanently eradicating the virus and preventing chronic complications. The impact of these new viral therapies open new perspectives for infected or with a new reactivation transplant recipients. Clinical Cases: We present two cases of deceased Donors after Brain Death (DBD), that were previously treated with antiviral agents resulting in negative RNA-HCV load but remaining positive serology for HCV Ab. Organs has been grafted in negative HCV recipients.

Donor 1: In 2016, a 55 years old female, DBD with a brain hemorrhage caused by a ruptured intracranial aneurism. Previous HCV infection, genotype 3 and treated in 2010 with Pegylated Interferon/ ribavirin (Peg/RBV) for 24 weeks, with a negative viral load since 2011.

Recipients: Liver: female, 41 years old, non viral liver cirrhosis, Child A with negative IgG HCVAb. At 3rd month after transplantation presents positive IgG HCV Ab with negative RNA–HCV. Right Kidney: male, 66 years old, with an IgA nephropathy. At 12 month after transplantation presents negative IgG HCV Ab with negative RNA–HCV. Left Kidney: Considered not suitable due to macroscopic aspect.

Donor 2: In 2016, a 72 years old female, DBD after brain hemorrhage. Previous HCV infection, genotype 1b and treated in July 2015 with Sofosbuvir/ Ledipasvir and Ribavirin (SOF/LDV + RBV) for 12 weeks, with a negative viral load since October 2015. Recipients: Right Kidney: female, 70 years old with an unknown nephropathy. At 12 month post-transplantation presents negative IgG HCV Ab with negative RNA–HCV. Left Kidney: female, 69 years old with a nephropathy since youth. 12 month after transplantation presents negative IgG HCV Ab with negative RNA–HCV. Liver: Considered not suitable due cirrhosis.

Conclusion: The presence of IgG HCV Ab in the liver recipient, but not in renal ones suggests plasmatic cell transference through liver transplant.

Clinical Liver Allocation

BOS216 OLDER DONORS FOR OLDER RECIPIENTS IN LIVER TRANSPLANTATION: A SAFE STRATEGY?

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Introduction: Old donors (≥70 years) have been associated with poor outcome in Liver Transplantation (LT). Due to the MELD driven allocation and the steadily rising average age of donors, older grafts are increasingly used for both older and younger (<70 years) recipients, but it is unclear which are the effects of these matching strategies on results after LT. We retrospectively compared outcome after transplanting old grafts into 'young' (<70 years) vs. 'old' (≥70 years) recipients in our center.

Methods: Donor and recipient demographics, transplant data, and outcomes were retrospectively compared in 'old donors to old recipients' LT (OOLT) vs. 'old donors to young recipients' LT (OYLT). Data are expressed as median (IQR).

Results: Between 1/2000–12/2015, 849 LT from brain death donor were performed. The incidence of 'old donors' and 'old recipients' was 13.5% and 7%, respectively. 21 (2.5%) OOLT and 94 (11%) OYLT were identified. Donor age was higher in OOLT than OYLT [79 years (76–82) vs. 76 (72–79); $p = 0.04$], but the Donor Risk Index did not differ. OOLT was performed mostly for HCC (OOLT 76.2% vs. OYLT 40.4%; $p = 0.004$) in recipients with lower labMELD score [OOLT 11 (8–16) vs. OYLT 16 (11–24); $p = 0.01$], and had a shorter cold ischemia time [OOLT 6.2 h (5–8) vs. OYLT 7.5 (6–10); $p = 0.02$]. The incidence of early graft dysfunction (OOLT 28% vs. OYLT 27%; $p = 1$), acute kidney injury (OOLT 9.5% vs. OYLT 20%; $p = 0.4$) and ischemic cholangiopathy (OOLT 9.5% vs. OYLT 8.5%; $p = 1$) did not differ. Hospitalization was shorter in OOLT [16 day (13–28) vs. 21 day (16–29); $p = 0.04$]. Five year patient (OOLT 57.4% vs. OYLT 76%; $p = 0.7$) and graft survival (OOLT 57% vs. OYLT 74.4%; $p = 0.2$) tended to be inferior but not significantly in OOLT.

Conclusions: Grafts procured from old donors can be safely allocated for LT regardless of recipient age matching strategy, granting favorable and comparable short- and mid-term results. Careful selection of older LT recipients seems relevant for a safe use of an old-to-old approach.

Clinical Liver Donation and donor types

BOS217 ANALYSIS OF INDICATIONS AND SURVIVAL IN THE LIVER RETRANSPLANT

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Background: Liver re-transplantation (re-LT) has an incidence of between 10% and 22% of total liver transplants (LT). These procedures are associated with increased risk and worse long-term survival than primary liver transplantation.
Methods: We present a retrospective study of 100 re-LT performed from January 1990 to December 2016 with a minimum follow-up of 6 months after re-LT. Patients were divided into two groups depending on the urgent/elective nature of re-LT analyzing the causes that motivated them and their survival.
Results: In our series, a total of 1234 TOH were performed in 1134 patients, with 100 re-LT; the rate of re-transplantation in our series is 8.1%.
Conclusion: The overall survival of the patients in our series was 11.10 $\pm$ 1.21 years. We found that the survival of urgently re-transplanted patients is greater than that of electively re-transplanted patients (15 194 $\pm$ 1.71 vs. 7.92 $\pm$ 1.10 days with p 0.02).

Clinical Liver Allocation

BOS218 RETROSPECTIVE ET-DRI SCORING IN A HIGH VOLUME LIVER TRANSPLANT CENTRE

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Background: The Eurotransplant Donor Risk Index (ET-DRI) has been developed to estimate graft survival following orthotopic liver transplantation (OLT), and can be helpful in the decision process of whether or not accepting a liver allograft.
Methods: We performed a retrospective analysis of all consecutive adult OLT performed between January 1st, 2007 and December 31st, 2013, split them in the 7 ET-DRI categories and analysed graft and patient survival according to different categories.
Results: In total, we included 399 patients in our analysis. The 3-years patient survival ranged between 78% and 88%, and the 3-years graft survival between 67% and 87%. 3-years patient survival rates for the different ET-DRI categories were 79% (category 1), 88% (category 2), 86% (category 3), 89% (category 4), 81% (category 5), 88% (category 6) and 78% (category 7). 3-years graft survival rates were 71% (category 1), 88% (category 2), 83% (category 3), 83% (category 4), 76% (category 5), 86% (category 6) and 67% (category 7). Regarding graft survival, there were two "outliers" compared to the expected scale. Category 1 and 6. Category 1 included only 16 patients, and was therefore not included in further analysis. In order to better identify possible center specific, donor associated risk factors for worse allograft survival, we split the group in patients with 3-years graft survival >83% and patients with 3-years graft survival <76%. We analysed all common donor associated risk factor including the ET-DRI factors using multivariate analyses. The only statistically significant factor associated with worse outcomes was extraregional allocation ($p = 0.045$), a factor already included in the ET-DRI. There were no other statistically significant factors influencing graft survival.
Conclusion: The "outliers" observed in our retrospective analysis point at important recipient associated factors which have to be included in the decision process when accepting or declining a liver allograft.

BOS219 PROGNOSTIC FACTOR FOR LIVER RE-TRANSPLANTATION: ANALYSIS OF A SINGLE-CENTER EXPERIENCE IN JAPAN

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Background: Liver retransplantation (re-LT) is the only effective therapy for irreversible failure of a liver graft. This study aimed to assess the results of re-LT for patients with graft dysfunction after primary liver transplantation at our institute.
Patients and Methods: From June 1990 to December 2015, a total of 1777 LTs were performed in at Kyoto University Hospital, in which 111 re-LTs were included. We evaluated the characteristics, survival and prognostic factors after liver re-LT retrospectively; indication, early (re-LT performed within 3 month after the last LT) or late, and graft volume.
Results: The number of DDLT/LDLT was 22/89 cases, and male/female ratio was 41/70. Average recipients' age was 22 y/o (10 month-68 y/o). Early re-LT was performed in 20 cases (18%). ABO incompatible cases were 31 cases. The patients' status was ICU bound in 30 cases (27%), and hospitalized in 64 cases (58%). The reasons for re-LT were as follows: rejection in 49 cases; recurrence of primary disease in 19 cases; vascular complications in 13 cases; other reasons in 17 cases. The indication for the initial LT was BA in 53 cases (49%), and PSC in 15 cases (14%), and acute liver failure in 11 cases (10%). After the law for the DDLT had changed in July 2010, the number of re-LT from deceased donor increased drastically from 5 cases (23% of re-LT) to 17 cases (77%) ($p < 0.0001$). 1-, 5-, 10-years survival after re-LT was 65%, 58%, 54% in all re-LT cases, respectively. Univariate analysis revealed early re-LT within 3 months (1-year survival: early 25%, late 74%; $p < 0.0001$), pre-transplant patient's status (1-year survival: ICU bound 33%, hospitalized 70%, at home 100%; $p < 0.0001$) and the era before April 2006 (1-year survival: 59% vs. 85%; $p = 0.0021$) were poor prognostic factors. Multivariate analysis showed that early re-LT was prognostic factor after re-LT (HR 2.6; 95% CI 1.2–5.6, $p = 0.010$).
Conclusion: The prognosis after re-LT became better; however, the prognosis of the early re-LT is poor.

Clinical Liver Donation and donor types

BOS220 OUTCOME OF LIVER TRANSPLANTATION FROM AGED DONORS >70 YEARS

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Introduction: The limited organ supply urged the use of liver allografts from donors >70 years. Traditionally, older donors have been regarded as high-risk transplants, but recent experience report on encouraging results. We analyzed our own experience using aged donor >70 years.
Methods: We used a retrospective analysis including 338 liver transplants in 310 adult recipients (>18 years) performed in 2000–2015, excluding live-donor and combined liver-kidney transplantation. The use of liver allograft from donors > 70 years was introduced in a later era, since 2008. Three groups were compared according to donor age: donors younger than 60 years. (200 patients), 60–69 years (65 patients) and >70 years (45 patients) with regard to long term survival and complications. Statistical analysis included Kaplan-Meyer survivals and Pearson chi square test.
Results: In the group of donors over 70 years, the mean donor and recipient age was 74.3 years (70–81 years.) and 57.8 years (22–74 years.), respectively. Mean cold ischemia was significantly shorter for recipients of liver donor >70 years; 6.38 vs. 8.41 h. for the rest of the patients ($p < 0.001$). Graft survival in recipient of a liver graft from donors >70 years was not statistically different from that of the other two groups (table). In recipients of grafts from donors > 60 years a significantly higher rate of vascular complication was noted ($p < 0.05$).
Conclusions: Adequate graft selection and maintenance of short cold ischemia, below 8 h allows use of liver grafts from donors older than 70 years, though a higher vascular complications rate may be expected.

	donor <60 years. (228 p.)	donor 60–69 years. (65 p.)	donor >70 years. (45 p.)
1 year graft survival	73.3%	70.1%	76.0%
5 year graft survival	71.0%	51.8%	66.1%
10 year graft survival	64.5%	43.7%	58.0%
biliary complications	44 (19.2%)	17 (26.1%)	9 (20%)
vascular complications	9 (7.4%)	6 (15.3%)	5 (13.3%)

Clinical Liver Allocation

BOS221 LIVER TRANSPLANTATION IN PATIENTS >65 YEARS – ANALYSIS OF LONG-TERM CLINICAL OUTCOME

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Background: Liver transplantation (LT) in older patients is controversially discussed in the literature. The aim of this study was to evaluate long-term outcome of patients receiving LT aged >65 years.
Methods: 65 patients >65 years receiving a liver transplant between 1989–2014 were included in this retrospective single-center study. Patients' characteristics and postoperative outcome were analysed.
Results: Overall 1- and 5-years-survival rates of patients >65 years were 74% and 51%. Patients with donor-recipient age difference ≥10 years ($n = 43$) showed significantly worse outcome compared to those with <10 years ($n = 22$, $p = 0.02$). Furthermore, patients with a postoperative rejection episode displayed significantly lower survival (19%, $p = 0.04$). Comparing the period from 1989–2004 (pre-MELD) to the period after MELD-implementation (2005–2014), revealed a significantly better survival in the later time period (1- and 5-year: 69%, 37% vs. 80%, 65%, respectively; $p = 0.03$). Patients' characteristics were equally distributed in both groups except for a less frequent postoperative rejection rate ($p = 0.02$), higher number of ATG-induction ($p = 0.01$) and a higher donor age ($p < 0.001$) after 2004. Comparing the survival of patients aged 18–65 years ($n = 1245$) to those >65 years, the younger patient cohort displayed a significantly better survival ($p = 0.01$). However, this correlation subsided when only the period from 2005–2014 was considered ($p = 0.99$).
Conclusion: LT in patients >65 years results in comparable survival to patients <65 years in the modern era. However, our data suggest that the donor age should be taken into account during organ allocation, as big age differences negatively impact postoperative outcome. Further studies are needed addressing donor-recipient age mismatch in LT.

Clinical Kidney Infection

BOS224 OUTCOME OF RENAL TRANSPLANTATION IN PATIENTS WITH HEPATITIS C AND HEPATITIS B COINFECTION

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Infections with hepatitis C (HCV) or hepatitis B (HBV) virus are associated with increased morbidity and mortality in renal transplant population. It is reasonable to expect worse results in cases of HCV and HBV coinfection, however, data about this topic is scarce. In the present study, we investigated prevalence, clinical course and outcome of renal transplantation in this group of renal transplant recipients.

A cohort of 1898 renal transplant recipients, transplanted from 1973 to 2017 was included in investigation. Demographic factors, graft survival, patient survival and complications were obtained from medical charts and records.

HCV and HBV coinfection was recorded in 12 patients (8 male), with median age at transplantation 39.5 (range 21 to 50) years, treated with dialysis for 7 (range 1 to 12) years. The last patient with HCV and HBV coinfection was transplanted in 2008. Nine patients had chronic glomerulonephritis, 1 polycystic kidney disease and 2 unknown primary kidney disease. HCV genotype was 1b in all patients. All patients received cyclosporine and low dose steroids, 5 were treated with azathioprine and 7 with mycophenolate mofetil). Eight patients had an episode of acute allograft rejection, 8 had hypertension, and 8 elevated liver chemistries. None of the patients developed posttransplant diabetes. Six patients had lost allograft 13 years after the transplantation (range 2 to 20 years), 5 patients died (3 developed liver failure, 1 had stroke, and 1 sudden death). One patient is still alive with functioning allograft, 14 years after the transplantation.

Our results demonstrate that patients with HCV and HBV infection may be successfully transplanted with careful follow-up. Liver failure was the major cause of death.

Clinical Liver Infection

BOS225 BACTERIAL ENDOCARDITIS IN LIVER TRANSPLANT PATIENTS: A SERIES OF 8 CASES

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Background: Bacterial infections occur in approximately 2/3 of patients in post liver transplantation (LT). The most prominent places are the abdomen, biliary tree, surgical wound, lungs and bloodstream. Endocarditis is rarely described in the literature.
Objectives: Describe the main clinical, microbiological and echocardiographic aspects, along with the evolution of patients submitted to liver transplantation who developed bacterial endocarditis in the period 2008–2016.
Material and Methods: We reviewed the clinical reports of liver transplant recipients who had a febrile condition with positive blood cultures and an echocardiogram with evidence of vegetations (Duke's major criteria).
Results: We identified 8 cases; the average age was 54.1 years. In six the cause of liver transplantation was chronic liver disease and in two cases it was familial amyloid polyneuropathy. In five patients, bacterial endocarditis occurred in early post-LT (<3 months). Prior to LT, one patient had biological aortic prosthesis, one patient had severe asymptomatic aortic regurgitation and three patients had a pacemaker; post-LT two patients required haemodialysis with multiple catheters. All patients had a transesophageal echocardiogram: the aortic valve was affected in seven cases, one had simultaneous mitral valve infection and one patient had a pacemaker infection. The microorganisms isolated were: *MRSA* ($n = 2$), *MSSA* ($n = 1$), *Pseudomonas aeruginosa* ($n = 2$), *Enterococcus faecium* ($n = 1$), *Enterococcus gallinarum* ($n = 1$) and *Corynebacterium striatum* ($n = 1$). Five patients underwent cardiac surgery. Five deaths occurred.
Conclusion: Bacterial endocarditis had high mortality and occurred in patients with predisposing risk factors, either pre or post-LT, particularly valve prosthesis previous valvulopathy, exposure to multiple invasive procedures or dialysis. We suggest a careful pre-LT assessment in patients with valvulopathy and systematically rule out endocarditis in patients on transplant list.

BOS226 EARLY POSTOPERATIVE INFECTIONS IN LIVER TRANSPLANTATION

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Introduction: Infectious complications in early postoperative period after liver transplantation (LT) are frequently a direct result of the surgical procedure. Here we evaluate our early postoperative infections following LT.
Materials and Methods: We retrospectively investigated all 561 LT performed between November 1988 and January 2017 in our center and evaluated all cases of infection during the first hospital stay from LT until discharge (mean 14 days). We classified the infections into 2 groups: non-surgical site infections (NSSI) and surgical site infection (SSI), including deep infections related to LT site and superficial infections related to skin and fascia of surgical site.
Results: In the 561 LT, we detected infections in 131 (23.3%; 60 adult, 71 pediatric). 56 had NSSI (42%), 67 had SSI (51%) and 8 had NSSI + SSI (6%). We stratified the consequences and treatment protocols of infectious complications according to the Clavien scale.

There was no mortality due to NSSI; of the 56 NSSI patients: 34 (60%) received antibiotherapy, 9 (16%) received other pharmacological treatment in addition to antibiotherapy, 7 (12%) required endoscopic or radiologic intervention, 6 (10%) recovered from single or multi organ dysfunction.

There was no mortality due to SSI; of the 67 SSI: 37 (55%) were treated with antibiotherapy, 29 (43%) required endoscopic or radiologic intervention to recover, 1 (1%) recovered from single organ dysfunction.

Of the 8 NSSI + SSI, we lost 4 (50%) in the early postoperative period after LT, 3 patients required endoscopic or radiologic intervention to recover, 1 patient recovered from single organ dysfunction.
Conclusion: Most early post-LT infections are related to surgical procedure, medical devices and early interventions. Initiation of appropriate prophylactic and therapeutic protocols at the right time decrease morbidity and mortality.

BOS227 EARLY INFECTIOUS COMPLICATIONS AND THE OUTCOME OF LIVING DONOR LIVER TRANSPLANTATION (LDLT)

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Background: Liver transplantation (LTx) has emerged over the past decades as the treatment of choice for patients with end stage liver disease. Survival after liver transplantation has improved over years due to advances in surgical techniques and reduction in allograft rejection. Despite measures such as the use of protective barriers, antimicrobial prophylaxis, and vaccination, post operative infection is still considered a major cause of morbidity and mortality after liver transplantation.
Objective: Evaluation of the effect of post LTx infection on the outcome of living donor liver transplantation (LDLT) regarding morbidity and mortality, and also to identify the possible risk factors for these infections.
Methods: This study included 100 Egyptian patients with post hepatitic cirrhosis who underwent LDLT. Patients were divided according to the development of post operative infections into 2 main groups; Group A: patients who didn't suffer any type of infection during the early post operative period (1st month), Group B: patients who suffered post LTx infection in the same period. According to the type of infection whether bacterial, viral and fungal this group was further sub divided into 3 subgroups.
Results: The rate of early complications & mortality were significantly higher among the group who developed infection especially for sepsis & biliary complications (p value <0.0001). The rate of blood and FFP transfusion and the duration of anhepatic phase were significantly higher in the group who developed infection (p value <0.005). The presence of HCC, Size of HCC >3 cm, serum bilirubin>4.4, fever>37.2, and CRP>17.5 could be considered as predictors of post operative infections by multivariate analysis (logistic regression).
Conclusion: Early post operative infections are the leading cause of morbidity and mortality in LTx.

BOS228 A RANDOMIZED, OPEN-LABEL, SINGLE-CENTER, PHASE II CLINICAL TRIAL TO EXPLORE THE SAFETY AND EFFICACY OF RECOMBINANT HEPATITIS B IMMUNOGLOBULIN

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Background: HBV immunoglobulin (HBIG) is a cornerstone of HBV prophylaxis, but currently available, plasma-derived polyclonal HBIG is not an ideal source of therapeutic antibody due to cost, limited availability.
Materials and Methods: This was a prospective, randomized, open-label, single-center study. Total 40 adult patients who were scheduled to undergo LDLT for HBV, each 20 for the low dose (50 000 IU) and for the high dose (80 000 IU) group, were included. The investigational product was recombinant HBIG (GC1102, Host cell: CHO DG44, expression vector: pRC12-HB-H4, pKC12-HB-L9, content: 10 000 IU/ml). The intravenous bolus injection of 50 000 IU or 80 000 IU of GC1102, was given during anhepatic phase. And the same dosage was administered daily, weekly and monthly during the post-LDLT 1st week, 1st month and 1st year, respectively. Including the first visit at which informed consent was obtained, subjects returned for a total of 20 visits during the 28-week of study period for the assessments of safety, efficacy and PK profiles of the study drug. This study was reviewed and approved by the IRB and was conducted according to the protocol in compliance with KGCP.
Results: Of 40 subjects, 29 (74.35%) completed the study, and 10 (25.64%) were prematurely withdrawn from the study. No patient of the 29 subjects who had completed the study and been included in the ITT population showed HBV recurrence. There was no serious adverse event related with study drug. The 3-compartment simulation model showed that the mean values of AUC, Cmax and Tmax was 1 227 9956 (IU h/l), 61 199 (IU/l), 138.6 (h) in low dose group, respectively; while in high dose group, the mean values of AUC, Cmax and Tmax was 1 960 818, 99 473, 116.4, respectively.
Conclusion: GC1102 would be effective in preventing recurrence of hepatitis B following liver transplantation.

Clinical Kidney Infection

BOS229 TREATMENT OF HEPATITIS C IN KIDNEY TRANSPLANT RECIPIENTS WITH DIRECT-ACTING ANTIVIRAL AGENTS NEWLY AVAILABLE IN JAPAN – PRELIMINARY REPORT

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Background: Hepatitis C virus (HCV) infection is a serious problem for kidney transplant patients, with a rate reported to be as high as approximately 10% in those on HD or who have undergone kidney transplantation in Japan. Interferon and ribavirin have been administered in the past, those treatments are now limited because of low efficacy and poor tolerability. Recently, new anti-HCV agents known as direct-acting antiviral agents (DAAs) were approved for use in Japan and have demonstrated high anti-HCV efficacy with a SVR. However, few studies of kidney transplant recipients who received DAAs treatment have been reported, because of drug interaction with calcineurin inhibitors as well as limited usage in patients with renal deterioration. In the present study, we examined the safety and effectiveness of DAAs for kidney transplant recipients in Japan.
Materials and Methods: 12 HCV-infected kidney transplant recipients were treated with DAAs. Their median age was 62 years and the average post-transplant period was 13.5 years, while the median eGFR was 60 ml/min. One patient had HCV genotype 2 and the others had genotype 1b. DAAs were administered as follows; the combination of ledipasvir + sofosbuvir was given to 8 and that of daclatasvir + ribavirin was given to 2, while 1 patient received sofosbuvir + ribavirin and 1 received ombitasvir + paritaprevir + ritonavir. We analyzed SVR rates, graft function, and adverse effects these patients.
Results: All patients except 1 achieved SVR at 24 weeks and 1 patient receiving SOF/RBV could not finish treatment because of anemia. No significant changes in eGFR were observed following DAAs treatment. Calcineurin inhibitor trough levels did not significantly change during therapy in 11 patients, while the patient who received OBV/PTV/r required CSA adjustment.
Conclusion: The present study findings suggest that interferon-free DAA therapy can be safely administered to HCV-infected kidney transplant recipients in Japan with good effectiveness.

Clinical Liver Infection

BOS230 HEPATITIS C CORE ANTIGEN TESTING IS A RELIABLE METHOD TO MONITOR ALL-ORAL THERAPY IN LIVER TRANSPLANT RECIPIENTS

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Aim: Here we investigated the diagnostic fidelity of HCV-core antigen assay for monitoring HCV therapy with direct acting antivirals in liver transplant recipients.
Methods: 45 transplant recipients treated with 48 direct acting antiviral (DAA)-based treatment courses were included in the study. Throughout and after end of treatment HCV-RNA and HCV-core antigen levels were assessed by PCR and immunoassay, respectively. Correlation between both tests was evaluated by linear regression (Pearson). Univariate analyses (Fisher's exact test, *t*-test and Mann-Whitney *U*-test, each were applicable) were performed to identify predictors of sustained virological response 12 weeks after end of treatment (SVR12).
Results: Of the 44 patients treated 19.4% had graft cirrhosis and 79.8% were treatment experienced. Patients received the following treatment regimen: SOF/LDV ± RBV (n = 19), SOF/RBV (N = 12), SOF/SMV ± RBV (n = 11), SOF/DAC ± RBV (n = 4), SOF/Peg-IFN/RBV (n = 1) and SMV/DAC/RBV (n = 1). There was a strong correlation between HCV-RNA and HCV-coreAg levels in the entire cohort ($r = 0.8279$; $p < 0.001$) and in the subgroup of patients treated with SOF/LKDV ($r = 0.8756$; $p < 0.001$). SVR12 was achieved in 44/48 treatment courses (91.7%) and in all 19 patients treated or re-treated with SOF/LDV. Three patients treated with SOF/RBV experienced a relapse

and one patient treated with SOF/SMV/RBV discontinued therapy prematurely. Therapy duration until HCV-coreAg negativity was significantly associated with SVR12 ($p = 0.005$). HCV-coreAg negativity, but not undetectable HCV-RNA at treatment week 2 predicted SVR12 ($p = 0.046$ and 1).
Conclusion: HCV-coreAg testing is a reliable and inexpensive method for monitoring DAA therapy in transplant recipients with a HCV re-infection of the graft.

BOS232 PRE-EMPTIVE POST- LIVER TRANSPLANT (LT) HCV TREATMENT WITH DAAS: PROOF OF CONCEPT OF A PILOT STUDY

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Background and Aims: The adoption of a "true" pre-emptive treatment with DAA has never been explored so far. In our pilot study, SOF + RIBA were administered starting on the day of transplant surgery.
Aim: To evaluate feasibility, safety and efficacy of a Sofosbuvir plus ribavirin post-LT preemptive regimen.
Methods: 45 consecutive HCV positive patients undergoing LT were prospectively enrolled for a 24 weeks SOF + RBV treatment. The first dose of SOF + RIBA was administered at graft implant, through N-G tube; HCV-RNA was tested at 1st, 2nd, 4th wk and then every 4 weeks until 24th weeks post-treatment.
Results: The baseline features of recipients/donors are shown in Table 1. At the time of the analysis, 24/45 reached SVR 12. At week 1, in 9% HCV-RNA was undetectable (NR), in 75% the viral load was <3 log. All patients achieved EOT response. At univariate analysis, advanced donor age showed a statistically significant correlation with viral load decay (slope: −0.02; correlation: −0.34; r-squared: −0.12; $p = 0.04$). By ITT analysis, SVR12 was 92% (2 relapses, both due to RBV withdrawal during treatment: 1 voluntary and 1 due to anemia). Five patients died for complications unrelated to DAA treatment during the post-operative period and 1 patient died for fibrosing cholestatic hepatitis after relapse. Acute rejection occurred in 12.1%. The peak of incidence of anemia (Hb < 9 g/dl) occurred at week 2 in 23% of patients); Blood transfusions (BT) were the first supportive care option followed by erythropoietin; from treatment week 12 no more transfusion were needed.
Conclusions: Our pilot study shows that a preemptive treatment strategy is a feasible strategy: adopting a "sub-optimal" RBV-containing regimen, SVR 12 was obtained in 92% (failures due to RBV-related anaemia). Based upon this data, a RBV-free regimen could warrant excellent result.

Table 1
Baseline features of recipients.

Age	52 [50-57]
Male sex (N%)	88%
BMI (kg/m^2)	24.5 [22.7-27]
Indication for LT	
ESLD	55%
HCC	45%
Median MELD at the time of LT	17 (14-22)
Median HCV-RNA at the time of LT	4.8 (4-5.1)
Genotype	
1a	16%
1b	23%
3	26%
4	35%
Experienced (%)	52%
Donors features	
Median age [95% UCL-LCL]	57 (52-71)
Anti-Hbc+ (N%)	16%
Median cold ischemia time	467 (360-506 min)
Immunosuppression regimen	
FK	45%
Cyclosporine	55%
Median ribavirin dose at the start	1000 mg/day

Clinical Kidney Infection

BOS233 EFFICACY AND TOLERABILITY OF INTERFERON-FREE REGIMENS FOR HEPATITIS C TREATMENT IN KIDNEY TRANSPLANT RECIPIENTS: TWO YEARS OF EXPERIENCE

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The development of direct-acting antiviral agents (DAAs) has allowed treating hepatitis C (HCV) in kidney transplant recipients (KTR) but data is limited.

We performed a retrospective analysis of KTR from our center with HCV treated with DAAs. Sustained virologic response (SVR) was defined as negative viral load (NVL) at 12 weeks post therapy.

We evaluated 19 KTR (57 ± 9 years old, 68% male) with a follow-up of 16 ± 6 months [2–26]. Four patients were diabetic and 16 were hypertensive. In all cases the graft was from a deceased donor and 6 had a second or third graft. Engraftment occurred 14 ± 8 years before [1–26]. Immunosuppression comprised FK506+ mycophenolate mofetil (MMF) + prednisolone (PDN) in 7 of the cases, cyclosporine A (CSA) + PDN in 5, CSA + MMF + PDN in 3, CSA monotherapy in 2 and FK506+ sirolimus in 1. The HCV load was log 6.2 ± 1.4 [1.6–7.4]. Ten patients presented genotype 1b, 5 genotype 1a and 4 genotype 3a. The FibroScan score was 1 in 8, 2 in 3, 3 in 4 and 4 in 4 patients. In 3 cases previous treatment with peginterferon was ineffective. The most commonly used DAAs regimen was sofosbuvir/ledipasvir ($n = 13$), followed by sofosbuvir + ribavirin ($n = 3$), ombitasvir/paritaprevir/ritonavir ($n = 1$), sofosbuvir/daclatasvir + ribavirin ($n = 1$) and ombitasvir/paritaprevir/ritonavir + dasabuvir ($n = 1$). The majority (95%) of patients had NVL at week 2 and all had NVL at the end of therapy. All achieved SVR. Graft and patient survival at last follow-up was 100%. A total of 8 cases (42%) worsened graft function and 3 (16%) increased proteinuria during or shortly after end of treatment. Only one had T-cell mediated rejection and treatment was suspended at week 3. In 10 patients calcineurin inhibitor (CI) dose adjustment was needed. Four patients on ribavirin needed exogenous erythropoietin. One patient with ascites switched to daclatasvir.
Conclusion: Our preliminary data support that DAAs are effective in KTR. Graft function and CI serum levels should be closely monitored.

Clinical Others Other

BOS234 IMMUNOSUPPRESSION THERAPY DURING TREATMENT OF CHRONIC HCV INFECTION WITH NEW ANTIVIRAL DRUGS IN LIVER AND KIDNEY TRANSPLANT RECIPIENTS

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Background: Interferon-free regimens are now considered as a treatment of choice in patients after organ transplantation with chronic hepatitis C (CHC), however influence of these new drugs on blood concentration of calcineurin inhibitors (CNIs) is not well explored. *The aim of the study* was: (1) to analyze the changes of tacrolimus (Tc) or cyclosporine A (CyA) blood trough level (Tc0 and CyA0 resp.) during therapy of CHC based on sofosbuvir (SOF) in kidney or liver transplant recipients (KTR, LTR) (2) to assess the safe frequency of Tc administration based on blood Tc0 during first three months of 3D regimen (paritaprevir/ritonavir/ombitasvir plus daclatasvir) in LTR.
Material and Methods: 64 HCV-infected patients (35 KTR, 29 LTR), were included to the study. In SOF-group, before the administration of first doses of antiviral drugs and after 4, 8 and 12 weeks of therapy, blood Tc0 (in 29 pts) or CyA0 (in 20 pts) was determined. Daily CNIs dosage was adjusted according to the current blood levels of CyA or Tc. In 3D-group, on days 3, 7, 10, 14, 28, 56, 84, the blood Tc0 was evaluated and the optimal frequency of Tc administration was calculated.
Results: In SOF-group, a significant decrease ($p < 0.001$) of initial blood Tc0 (−43.8 ± 15.7%) and CyA0 (−51.1 ± 14.8%) was found. The mean blood Tc0 decreased from 7.7 ± 1.7 ng/ml at the beginning to 4.3 ± 1.7 ng/ml during treatment and mean blood CyA0 decreased from 111.1 ± 35.2 ng/ml to

50.7 ± 14.1 ng/ml and in majority of pts, described changes were already found after the first month of therapy. In 3D-group, in all pts during first two months of therapy, the safe frequency of Tc administration was determined (mean interval between the doses was 8, 9 days; range 7–14 days).
Conclusions: 1. SOF-based therapy leads to the significant decrease of CyA0 and Tc0 and early modification of CyA and Tc dosage is mandatory 2. Frequency of Tc administration should be individually established during the antiviral therapy with 3D regimen.

Clinical Kidney Infection

BOS235 SOFOSBUVIR-CONTAINING ANTIVIRAL TREATMENT FOR CHRONIC HEPATITIS C VIRUS INFECTION IN RENAL TRANSPLANT RECIPIENTS: A SINGLE-CENTER INITIAL EXPERIENCE

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Background: The treatment of HCV infection in renal transplant recipients is always a dilemma before the development of direct-acting antiviral agents. Recently, Sofosbuvir-containing regimen has been used for the treatment of chronic HCV infection. But little is known about the efficacy and safety for infected renal transplant recipients.
Methods: Single-center and retrospective study of HCV-infected renal transplant recipients receiving Sofosbuvir with Ledipasvir or Daclatasvir was conducted. All patients were separated into two groups. Group 1 included seven patients with renal allograft failure who received a low-dose Calcineurin inhibitor-based regimen. Group 2 included eleven patients with functioning renal allograft who received a higher-dose Calcineurin inhibitor-based regimen than group 1.
Results: Six (85.7%) patients were infected by HCV genotype 1b in group 1 and eight (72.7%) patients in group 2. Others were infected by genotype 2. Median treatment duration was 12 (12–24) weeks. All patients achieved on-treatment response, with a mean time of 2.3 ± 1.3 weeks in group 1 and 1.6 ± 0.5 weeks in group 2. No one was re-infected in both groups and all patients achieved sustained virological response at 12 weeks after treatment cessation. In group 1, nausea was occurred in one patient (14.3%) and transient bilirubin elevation was occurred in one patient (14.3%). In group 2, mild edema of lower limbs was occurred in three patients (27.3%) and transient bilirubin elevation was occurred in one patient (9.1%). Transient serum creatinine elevation was occurred in two patients (18.2%) with abnormal renal function. All adverse events were CTCAE grade 1 and recovered after treatment cessation.
Conclusions: Treatment with Sofosbuvir-containing regimen in HCV infected renal transplant recipients is highly effective and well tolerated, which offers a new era for the effective treatment of a variety of transplant recipients suffering from chronic HCV infection.

Clinical Liver Infection

BOS236 INFLUENCE OF DAA TREATMENT ON WAITLISTING AND TRANSPLANT RATE (TR) FOR HCV-RELATED LIVER DISEASE: PRELIMINARY RESULTS OF A SINGLE CENTER EXPERIENCE

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Background and Aim: The availability of DAAs has allowed the treatment of HCV infection in the setting of OLT either before, during the waiting period and after LT. Therefore, a reduction of HCV prevalence, a relative increase of HCV transplant for HCC rather than ESLD and increasing waitlist removal for improvement should be expected. We aimed to assess the prevalence of HCV-related listed and transplanted pts from 2005 to 2016 and the improvement rate (IR).
Methods: From Jan 2005 to Dec 2016, 823 pts were consecutively listed at our centre (76% were transplanted). We identified 3 groups (G): GA-IFN age (2005–2011); GB-First Generation DAA (2012–2014) and GC-Second generation DAAs (2015–2016). Data were retrospectively analyzed.
Results: The mean prevalence of pts listed for HCV (both ESLD + HCC) in GC (31%) was lower than in the other group, although the difference was not significant (GA vs. C: p = 0.61; GB vs. C: p = 0.06). A decreasing number of pts listed for HCV-ESLD (GA: 38%; GB: 42%; GC: 32%) and an increase of HCV-HCC (GA: 54%; GB: 55%; GC: 58%) was observed in the last two years (p=ns). 219 pts were transplanted for HCV-related liver disease. The TR for HCV-ESLD was stable during the observation (from 30%-GB-up to 36%-GC, p = 0.5). The TR for HCV-HCC was significantly lower in GC (50%) than in GB (56%; p = 0.02). The ratio HCV-OLT/overall listed pts achieved a nadir in GC (20%) significantly lower than in GB (33%; p = 0.008) and GA (28%; p = 0.056; GC vs. GA + B-29%; p = 0.02). The ratio HCV-OLT/HCV-listed pts showed a progressive decrease with a significant difference between GA and GC (GA: 79%; GB: 69%; GC: 61%; GA vs. C: p = 0.02; GB vs. C: p = 0.09; GA vs. B: p = 0.09). The IR of HCV waitlisted pts in the last 2 years was higher than in the others (GC: 15%-all DAA treated-vs GB: 1%; p = 0.02) vs. GA (7%; p = 0.07).
Conclusions: Our data shows a clear trend toward an overall reduction of HCV prevalence in pts listed per OLT after just 2 years of DAAs, with a relative increase of HCC rather than ESLD. The IR observed in waitlist treated pts is consistent with the recent literature.

BOS237 EFFICACY AND SAFETY OF DIRECT ACTING ANTIVIRALS THERAPY IN HEPATITIS C REACTIVATION POST LIVER TRANSPLANTATION

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Background: Interferon-free therapies became treatments of choice in subjects with HCV reducing the problem of graft dysfunction after the recurrence of hepatitis C virus (HCV) post liver transplantation (LTx). Here we analyze our experience with DAAs (direct acting antivirals) in liver recipients (LR) treated in four Polish liver transplant centers since the end of 2015. Material and Methods

146 LR (68% males, mean age 56±10 years, median time after LTx: 2 years, 28% cirrhotics, 48% non-responders, median viremia of 1.8x106 IU/ml) predominantly infected with GT1b (90.2%) followed by GT4 (4.2%), GT3 (3.5%) and GT1/1a (2.1%) were included. 73% of pts were treated with sofosbuvir-based therapy (SOF/ledipasvir ± ribavirin (RBV) for GT1 and GT4 and SOF/RBV for GT3) and 27% of pts with 3D regimen (paritaprevir/ritonavir/ombitasvir ± daclatasvir ± RBV) for GT1 and GT4. The effectiveness of therapy was analyzed by assessing of end-therapeutic response (ETR) and sustained virologic response (SVR12/24) defined as an undetectable serum HCV RNA level at the end of therapy and after 12 or 24 weeks after treatment, resp.
Results: ETR was achieved in 99% (n = 135) and SVR*12/24*, 97% (n = 99) of pts. SVR12/24 in SOF (n = 63) and 3D (n = 36) group was 97% in both groups. In GT1b group, 99% and 96% of pts achieved ETR and SVR12/24 resp. The therapy was stopped in 5 pts (liver failure, hepatotoxicity, deterioration of kidney function, recurrent vomiting). Weakness (34%), fatigue (30%) and headache (18%) were the most common adverse events. Frequency of tacrolimus (Tc) administration was individually established during the therapy with 3D regimen and mean interval between the doses was 9 days (range 7–14 days). In SOF group the correction of Tc dose was necessary in 38% of pts and increasing the dose of Tc was required 83% pts.
Conclusions: Therapy with DAAs in liver transplant recipients is safe and highly effective. Immunosuppression therapy has to be closely monitored and adjusted during and after therapy.

Clinical Kidney Metabolic complications

BOS238 ROLE OF PARICALCITOL IN DEVELOPMENT OF DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION

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Introduction: *Diabetes mellitus* after transplantation is a frequent and serious complication in organ transplantations (PTDM). One of the possible risk factors for development of PTDM is proteinuria.

Materials and Methods: In the group of 167 patients – non-diabetic, we identified several risk factors for PTDM (body mass index, proteinuria, age at the time of transplantation, and positive family history). In stage two of monitoring both the control group and the group of PTDM patients, we determined also the following: the value of intact parathormone, the value of calcium, phosphorus, D vitamin, and type of treatment (cholecalciferol, cinacalcet, paricalcitol).
Results: In the homogenous group of patients, from the aspect of immunosuppression, we detected the following risk factors for PTDM: D vitamin <30 ng/ml [HR 1.3167; 95% CI 1.0057–1.8741 (p = 0.0322)], proteinuria > 0.15 g/day [HR 3.0785; 95% CI 1.6946–5.5927 (p = 0.0002)], phosphorus at the time of transplantation > 1.45 mmol/l [HR 0.0821; 95% CI 0.0042–1.5920 (p = 0.0439)] – Table 1. We found out that the significantly lowest proteinuria and the lowest occurrence of PTDM was recorded in the patients who took paricalcitol (p < 0.0001) before and after transplantation. In the group of patients with and without proteinuria, there was no significant difference between the treatment by ACEI or sartans (p = 0.8955).
Conclusion: In our group, proteinuria and hyperphosphatemia represent an independent risk factor for development of PTDM. A significantly lowest occurrence of PTDM and proteinuria was recorded in the group of patients who were treated by paricalcitol.

BOS239 SODIUM/GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR FOR DIABETIC KIDNEY TRANSPLANT (KT) PATIENTS

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SGLT2 inhibitor is a newly introduced hypoglycemic drug that inhibits glucose reabsorption at proximal tubule. A recent RCT in CKD patients showed a long-term renoprotective effect, by a decrease in hyperfiltration as a consequence of increased distal sodium delivery with tubuloglomerular feedback (NEJM 375:323, 2016). This result seems relevant to KT patients where reduced nephron mass may suffer from hyperfiltration that jeopardizes long term graft survival. But the experience of this drug in KT patients is limited and there are concerns of acute graft dysfunction largely due to volume depletion by osmotic diuresis and lower urinary tract infection. The aim of this study is to evaluate the safety and efficacy of SGLT2 inhibitor in KT patients.

Twenty-five KT patients were treated with dapagliflozin 5 mg/d. Three patients had type 1 DM and 7 had NODAT. Sixteen patients were on insulin with or without oral agents. Median posttransplant months were 72 (9–262). Diuretics were stopped before the initiation of study drug.

Baseline HbA1c was 7.9 ± 1.3%, decreased significantly at 3 (7.4 ± 1.1%, p = 0.01) and 6 (7.4 ± 1.0%) months (M). Body weight decreased significantly from 72.2 ± 22.1 to 68.1 ± 22.0 (p = 0.000) kg at 12 M. Two patients could stop insulin and another 4 patients could reduce ≥20% dose of insulin. eGFR did not change significantly (71.1 ± 20.1 ml/min at baseline, 71.5 ± 25.8 at 12 M). Clinically apparent acute graft dysfunction was not observed. Office blood pressure also was not changed significantly but 10 of 24 patients had a decrease in number and/or dose of anti-hypertensives. No significant change in urine albumin-creatinine ratio at 1 year. Six patients discontinued study drug due to acute cystitis in 2, weight loss in 1 and lack of efficacy in 3.

SGLT2 inhibitor seems to be beneficial in glucose control of KT patients, with acceptable safety profile. Further studies are clearly needed to determine the possible long-term renoprotective effect in this patient population.

Clinical Kidney Cardiovascular complications

BOS240 THE PREVALENCE AND PREDICTORS OF AORTIC ROOT DILATATION IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background: The aim of this study was to assess the prevalence of enlarged aortic root (AR) and compare the effect of immunosuppressive (IS) regimens based on either mammalian target of rapamycin inhibitors (mTORi) or calcineurin inhibitors (CNI) on the risk of aortic root dilatation (ARD) in renal transplant patients (pts).
Methods: The study included 102 kidney transplant recipients. Pts with a valvular disease were excluded. The remaining 90 pts were divided into 2 groups: 40 pts treated with mTORi and 50 pts treated with CNI. Echocardiography, laboratory and clinical markers of cardiovascular risk (CR) were assessed in both groups. We calculated predicted ARD for each patient according to the equation for adults subjects published by Devereux et al.: 2.43 + [age (years) × 0.009] + [body surface area (m^2) × 0.461] – [sex (1 = M 2 = F) × 0.267]
Results: The enlargement of ARD in comparison to the predicted value of ARD was found in 66 pts (73%). It was more frequent in pts treated with mTORi (80%) than CNI (68%) (p < 0.05). Moreover, patients treated with mTORi had significantly larger ARD (p = 0.001), higher left ventricular (LV) diastolic (p = 0.04) and systolic diameter (p = 0.01) than patients on CNI. The incidence of cardiovascular disease (p = 0.04), level of total cholesterol, LDL, triglycerides (p < 0.02), were higher and time of renal replacement therapy (RRT) was longer among pts treated with mTORi (p < 0.003). There were no differences in age, gender, and other clinical parameters between the groups. The multivariate analysis revealed that enlargement of ARD was independently associated with IS regimen based on mTORi (p < 0.002) and not associated with time of RRT and other examined CR factors.
Conclusion: The prevalence of ARD was high in kidney transplant pts. Extent of enlargement of AR diameter associated with higher LV systolic diameter was greater in pts with IS therapy based on mTORi.

Clinical Kidney Metabolic complications

BOS241 THE EFFECT OF URIC ACID LEVELS ON SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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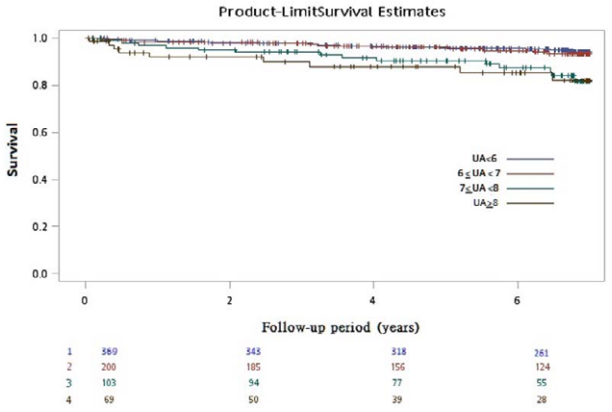
Background: Uric acid (UA) has been linked to hypertension, coronary artery disease and renal dysfunction. However, no specific data on the relationship between serum uric acid and kidney transplant recipient survival remains limited and deserves further investigation. The aim of study is to compare clinical outcomes in different category levels of uric acid in kidney transplant recipients.
Methods: We conducted a hospital-based cohort study using data from the period 2010–2015. All participants were stratified into four groups: Those with low UA levels (<6.0 mg/dl), normal UA levels (6–6.9 mg/dl), modestly elevated UA levels (7–7.9 mg/dl), and elevated UA levels (≥8.0 mg/dl). Cox models were used to estimate hazard ratios (HR) of all-cause mortality, after adjusting for underlying demographic covariates.
Results: This study included 742 kidney transplant recipients. Compared with the reference of UA 6–6.9 mg/dl, overall mortality risks were significantly highest in the high UA of 7–7.9 mg/dl (HR, 2.63; 95% confidence interval [CI], 1.20–5.93). Kaplan-Meier curves found that subjects with high and modestly high UA levels were associated with a higher risk of all-cause mortalities compared to those with normal or low UA levels.
Conclusions: Compared to low or normal UA levels, high uric acid levels were associated with a higher risk of all-cause mortality.

UA levels	HR (95% CI) Model 1	HR (95% CI) Model 2	HR (95% CI) Model 3
<6	0.87 (0.42–1.88)	0.84 (0.41–1.83)	0.75 (0.35–1.67)
6–6.9	Reference	Reference	Reference
7–7.9	2.63 (1.20–5.93)	2.35 (1.07–5.33)	2.35 (1.06–5.32)
>8	3.11 (1.25–7.53)	3.89 (1.56–9.50)	3.18 (1.15–8.30)



BOS242 HIGH LEVELS OF PARATHYROID HORMONE AFTER ONE MONTH OF RENAL TRANSPLANTATION ARE RELATED TO LONG TERM GRAFT LOSS

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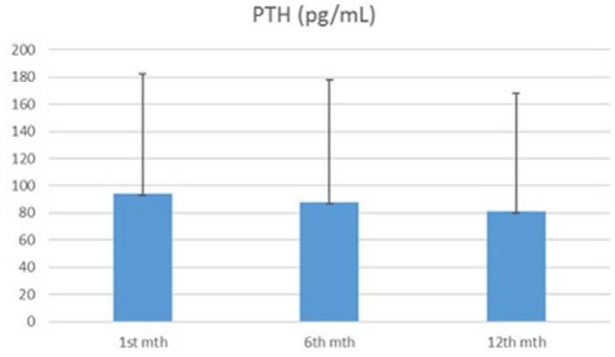
Background: Renal transplantation (RTx) only partially corrects certain metabolic alterations, especially in mineral metabolism (MM). Our study aims to examine the effect of RTx during the 1st year of RTx on MM parameters and to evaluate the factors mostly related to long term graft outcome.
Material and Methods: In 531 RTx pts (age: 48[39; 58] years – 303 males), transplanted in our unit between 2004 and 2014, clinical parameters, blood and urinary samples were collected before RTx and at 1, 6, 12 months after RTx. Median follow up was 7[2–12] years.
Results: Eighty-four percent of patients received a kidney from a deceased donor; 72% and 20% of patients were respectively treated with haemodialysis and peritoneal dialysis before RTx. Time of dialysis was 48[30–71] months. In the overall cohort MM parameters before RTx were: Ca 9.3[8.8–9.8] mg/dl, P 5.0[4.05–5.85] mg/dl, iPTH 205[123–443] pg/ml, ALP 106[66–170] U/l. Cold ischemia time (CT) was 13[11–16] h. In 13% of patients DGF was reported, and 13% of patients had at least one episode of rejection during the 1st year of RTx.

During the first year of RTx 6% of patients received cinacalcet. Thirty-five percent of patients were treated with active vitamin D, whereas in 11% of patients were supplemented with natural vitamin D alone. In the 1st year of RTx, a significant reduction of iPTH levels was observed (Figure 1 – $p = 0.005$). In the course of the follow up time, 66 pts restarted dialysis (D+). Compared to patients with a functioning graft (D–), D+ had longer CT ($p = 0.01$) and at the three time points considered, worst renal function, higher levels of urinary protein excretion and of iPTH. A significant difference in 1st year rejection prevalence was found ($p = 0.001$) between the two groups. In multivariate analysis only iPTH at 1st month and not iPTH at 12th month resulted independently related with graft loss ($p = 0.03$).

Using ROC curve, we evaluated the discriminatory power in predicting graft outcome for: 1st month eG



Clinical Others Other

BOS243 THE INCREASING CLINICAL BURDEN OF ACUTE KIDNEY INJURY IN NON RENAL SOLID ORGAN TRANSPLANT RECIPIENTS: A 15 YEAR RETROSPECTIVE ANALYSIS

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Introduction: Acute kidney injury (AKI) is a frequent complication in critically ill patients admitted to intensive care units complicated by high mortality and progression toward chronic kidney disease (CKD). Only few studies evaluated AKI incidence in non renal solid organ transplant (NRSOT) recipients. Aims of the study: (1) a 15-year retrospective analysis of AKI incidence in nrsot; (2) to identify the impact of aki on outcome and progression toward CKD.
Methods: Retrospective analysis of the percentage of nrsot in AKI population treated by renal replacement therapies (RRTS). Evaluation of rifle and sofa scores and severity index ATN_ISS at rrt start. Evaluation of the percentage of aki requiring rrt in nrsot population and for single transplanted organ (liver, heart or lung graft). renal function: evaluated at 30 days.
Results: In 2000–2015, we treated by RRT 2756 critically ill patients with AKI (12416 total sessions). nrsot recipients: 402/2756 (14.6%). We treated by RRT 10.8% of all patients subjected to liver transplantation, 27.5% of heart transplanted patients and 26.2% of lung transplanted patients. nrsot patients' characteristics: age 59.2 years (SD 7.6), male 62.5%, serum creatinine 3.76 mg/dl (SD 1.34), number of organ failures 3.7 (SD 1.87) and ATN_ISS score 0.68 (SD 0.16). main cause of aki in nrsot patients was sepsis (52.5%), associated with high mortality, multiple organ failures and difficult management of the immunosuppression. Overall mortality in nrsot patients was 42.6% (38.5% for liver, 48% for heart and 41.5% for lung transplant recipients, respectively). Mean serum creatinine at the end of the study period: 2.43 mg/dl (2.06 mg/dl in liver, 2.42 mg/dl in heart and 2.82 mg/dl in lung graft recipients).
Results: In conclusion, our 15-year retrospective analysis revealed a continuous increase of AKI incidence in the nrsot population. The main cause of AKI was sepsis which was associated with high mortality and with progression toward ckd in survivors.

Clinical Liver Cardiovascular complications

BOS244 PRE AND EARLY POST TRANSPLANT RISK FACTORS OF CARDIOVASCULAR EVENTS AFTER LIVER TRANSPLANTATION

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Background: Cardiovascular events (CVE) are among the most important causes of death after liver transplantation (LT), and their incidence is expected to increase in the next years. Risk factors for CVE have not been extensively investigated. We aimed to describe the incidence of CVE during the first year after LT, as well as to evaluate pre-transplant and early post-transplant risk factors.
Methods: We retrospectively evaluated all patients who underwent LT at our centre between January 2012 and December 2015. Cardiovascular risk factors before transplantation and during the first year after LT were studied, as well as immunosuppressive therapy and graft and kidney function during transplant admission. Major cardiovascular events (coronary artery disease, cerebrovascular disease, heart failure, peripheral artery disease, arrythmia) were recorded.
Results: 257 LT recipients (70% male, median age 57 years, median MELD score at LT 20 points) were included. Before LT, diabetes, arterial hypertension, dyslipidemia and smoking were present in 24%, 24%, 10% and 54% of the cohort, respectively. All risk factors except smoking significantly increased during the first year after LT. Eleven patients (4%) presented major CVE during the first year after LT. The number of pre-transplant risk factors was significantly associated with the incidence of CVE one year after LT, ranging between 2% for those with 0/1 risk factors to 14% for those with 4 risk factors ($p = 0.02$). At LT discharge, only the presence of renal failure was significantly associated with CVE (OR 4.3, $p = 0.026$).
Conclusion: Pre-transplant cardiovascular risk factors have a significant and additive impact on the development of CVE during the first year after LT, while the presence of renal failure during LT admission is also associated with CVE. Our results would support the investigation of the impact of renal-sparing immunosuppressive regimens in the incidence of CVE, particularly in patients with pre-LT risk factors.

Clinical Liver Metabolic complications

BOS245 PREDICTORS OF POST-TRANSPLANT SEVERE STEATOSIS IDENTIFIED BY FIBROSCAN WITH CONTROLLED ATTENUATION PARAMETER

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Background: The prevalence of post-transplant metabolic syndrome varies from 44% to 58%. The rates of steatosis and steatohepatitis are 20% and 32%, respectively. However, data about modern noninvasive liver graft assessment, such as transient elastography (TE) and controlled attenuation parameter (CAP), in order to detect hepatic steatosis are limited.

Methods: We characterized 44 LT recipients by TE and CAP and correlated the results with clinical and biochemical risk factors. Multiple regression analysis was performed. The cut-off value used for S3 steatosis was 300 dB/m.
Results: There were 30 men (68.2%), median age 58 years, median time since LT 35.1 months; 29 patients had cured HCV following therapy with DAA after LT and 15 patients were transplanted for other liver diseases. At TE the median liver stiffness value was 5.6 kPa and the median CAP was 289.5 dB/m. There is a moderate correlation between APRI score and liver stiffness ($r = 0.5$, $p = 0.001$). Independent predictors for severe steatosis S3 after LT were: high BMI ($p = 0.0004$), increased skinfold thickness ($p = 0.0008$), increased waist circumference ($p = 0.0003$), a higher thoracic perimeter ($p = 0.004$) and recurrent HCV hepatitis although with sustained virological response ($p = 0.02$). None of the biochemical parameters predicted presence of post-transplant steatosis.
Conclusion: Severe steatosis following LT is more frequent and should be screened in HCV recipients and with a higher percentage of body fat, even in the presence of normal biochemical parameters.

BOS247 LIVER TRANSPLANTATION AMELIORATES ADIPONECTIN DISTURBANCES IN ALCOHOLIC LIVER CIRRHOSIS

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Background: Adiponectin (ADN), the most abundant adipose-specific secretory protein, exhibits insulin-sensitizing properties and is thus inversely correlated with diabetes and metabolic syndrome. Paradoxically, patients with liver cirrhosis, an insulin resistant state by itself, are observed to have aberrant ADN serum levels, not associated with parameters of body composition, free fatty acids or insulin levels. The aim of this study was to explore the dynamics of standard metabolic parameters and ADN serum levels before and after liver transplantation (LT) for alcoholic liver disease (ALD).
Methods: A total of 29 consecutive ALD adult patients (mean age 57.44 ± 7.98 years, 79.3% male) were included. Patients with overt diabetes prior to LT were excluded. Parameters (body mass index (BMI), fasting blood glucose (FBG), glycosylated haemoglobin (HbA1c), insulin sensitivity, insulin resistance (IR), lipid profile) were evaluated at 3 time points (prior LT, 3- and 6-months post LT). IR was assessed by the Homeostasis Model Assessment 2 (HOMA-2) model and ADN concentrations were determined by validated enzyme-immunoassay methods.
Results: LT induced significant metabolic changes, with an increase of FBG, HbA1c, insulin sensitivity, triglyceride and cholesterol levels ($p = 0.018$; $p < 0.001$; $p = 0.009$; $p < 0.001$; $p < 0.001$, respectively), while a decrease of c-peptide and insulin levels, beta cell function, IR, and ADN was noted ($p = 0.045$; $p = 0.001$; $p < 0.001$; $p = 0.002$; $p = 0.001$, respectively). BMI was unaffected during the follow-up and no significant metabolic changes were observed between 3 and 6 months post LT.
Conclusions: LT elicited the reduction of IR with probable consequent alleviation of beta-cell function and insulin levels. Levels of ADN also decreased, possibly reflecting re-establishment of adipocytokine homeostasis significantly affected by cirrhosis. Further studies are needed to elucidate the complex interplay of adiponectin and metabolic alterations after LT.

BOS248 UNUSUAL ONSET OF DE-NOVO NEUROLOGIC DISTURBANCES IN WILSONIAN SIBLINGS AFTER ORTHOTOPIC LIVER TRANSPLANTATION: A CASE REPORT OF THREE SISTERS

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Background: Wilson's Disease (WD) is an autosomal disorder of copper metabolism which results in progressive liver cirrhosis, neurologic impairment, and renal malfunction. Although WD is rare in number, it accounts for 6%–20% of emergency Liver Transplantations (LT) due to its rapid deterioration. This study is to present two of three sisters with WD who developed severe neurologic complications after orthotopic liver transplant.
Case Presentation: Three 28, 25, and 19-year-old sisters who were known cases of WD cirrhosis and normal neurologic status underwent LT from deceased donors. While the first and third sisters developed severe new-onset neurologic disabilities 6 and 8 months after transplantation respectively, the second sibling showed no symptoms. Pre-transplant magnetic resonance imaging of brain revealed hyperintensity in the bilateral basal ganglia particularly in the caudate nucleus, putamen, and globus pallidus in T2 and fluid-attenuated inversion recovery sequences for both involved patients. Ceruloplasmin, copper, and 24 h urinary copper excretion at diagnosis were 13 and 12.9 (mg/dl), 26 and 32 (μg/dl), and 9 and 21.8 (μg) for the first and third sisters, respectively. Post-transplant neurologic findings were ataxia, dysarthria, dysphagia, sialorrhea, and tremor. In addition, unilateral blepharoptosis was observed in the youngest sister. Continuous administration of a chelating agent (mainly zinc sulfate) was considered against copper toxicity. Neurologic symptoms improved significantly 6–8 months after transplantation.
Conclusion: Although published literatures indicate that better pre-transplant conditions appeared to be advantageous in gaining better outcomes of patients with WD, but close monitoring of neurologic symptoms remains as an important area during the long-term post-transplant course. Furthermore, as new-onset neurologic disabilities in WD following LT are not expected, this phenomenon needs to be more studied in these siblings.

BOS249 ACUTE KIDNEY INJURY AFTER LIVER TRANSPLANTATION DOES NOT AFFECT PATIENT'S MORTALITY

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Introduction: Acute kidney injury (AKI) after liver transplantation is not uncommon. Several literatures show greater number of complications and high mortality rates with AKI after liver transplantation. The goal of this study was to determine the incidence of AKI during the early posttransplant period and mortality in patients undergoing liver transplantation in our hospital.
Patients and Methods: We retrospectively reviewed the medical records of all patients aged >18 years undergoing liver transplantation from March 2002 to September 2013. AKI was defined as an elevation of serum creatinine 1.5 times above the baseline or an absolute serum creatinine level >2 mg/dl. The exclusion criteria were hepatorenal syndrome at the time of transplantation and chronic renal failure with hemodialysis before liver transplantation.
Results: Of 70 selected patients, 20 patients (28.6%) developed AKI after liver transplantation, with 7 patients (35%) requiring renal replacement therapy (RRT). All the patients with AKI requiring renal replacement therapy could wean from hemodialysis. 1-year survival rates were 90% without AKI and 80% with AKI, respectively. But, there were no statistical significance ($p = 0.265$; odds ratio, 2.25). Among patients who underwent RRT, the 1-month mortality rate and the 1-year mortality rate were significantly high compared with the other remaining patients
Conclusions: There was a high incidence of AKI in patients undergoing liver transplantation and there was no survival difference between AKI group and no-AKI group. But the patients who require RRT show significantly low survival.

BOS250 EXTENDED RIGHT LIVER GRAFT AND THE FATE OF SEGMENT IV: NO SPLIT DECISIONS

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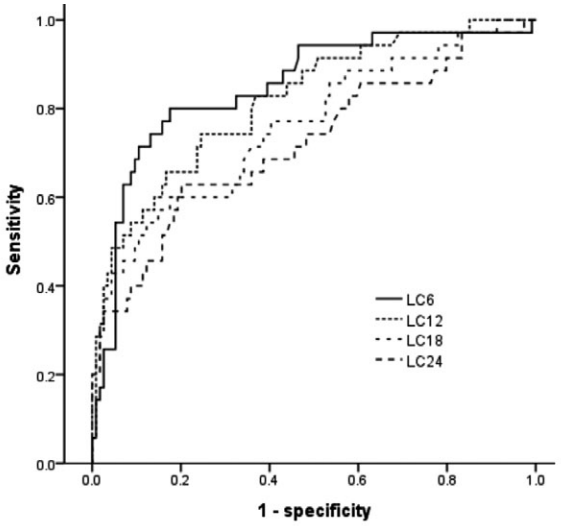
University Of Ghent, Belgium

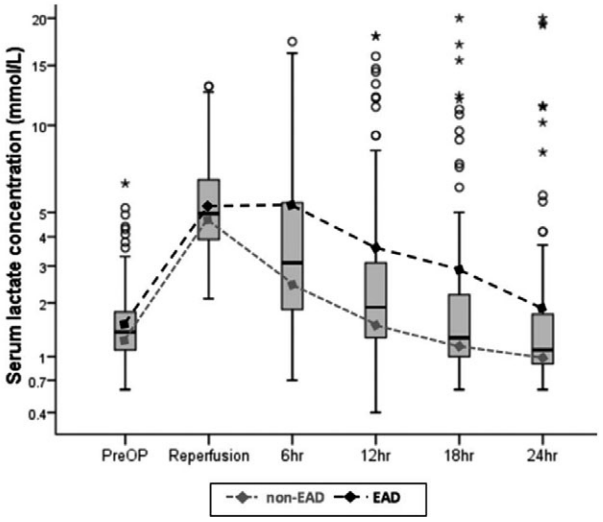
Background and Aims: Split-liver transplantation is a curative treatment for end-stage liver disease with excellent long-term outcomes. The extended right liver graft is grafted to size-matched acceptors. Choice in dissection plane has a variable influence on the separate liver grafts and the post-transplantation outcome. We wanted to correlate biliary and other complications to the presence of the segment IV artery.
Methods: We performed a single-center retrospective study in a liver transplant unit. We analysed 35 extended right liver grafts in the context of split liver transplantation. Operations were conducted between January 2000 and December 2014. Data were analyzed using the Chi-square and Fisher's exact test.
Results: Our population consists of 16 male (45.7%) and 19 female (54.2%) patients. Two patients were minors, 33 were adults. Segment IV arterialisation was interrupted in 12 patients (34.2%). Segment IV arterialisation is not significantly correlated with biliary complications ($p = 0.464$), bilomas ($p = 0.681$), segment IV infarction ($p = 0.151$), portal thrombosis ($p = 0.355$), retransplantation ($p = 0.385$) and reinterventions ($p = 0.575$).
Conclusions: These data show the indifference of the arterialisation of segment IV. Biliary and other complications occur whether or not segment IV still has its own artery. To complete our knowledge of the role of segment IV in extended right liver grafts, these data need to be compared to flow rates and pressure gradients in the hepatic artery. These aspects could give new directions in the approach of split liver transplantations.

BOS251 CLINICAL SIGNIFICANCE OF LACTATE CLEARANCE FOR THE DEVELOPMENT OF EARLY ALLOGRAFT DYSFUNCTION AND SHORT TERM PROGNOSIS IN DECEASED DONOR LIVER TRANSPLANTATION

Deok Gie Kim[1], Jee Youn Lee[1], Su-Kyung Kwon[1], Jae Geun Lee[1], Dai Hoon Han[1], Dong Jin Joo[1], Man Ki Ju[2], Gi Hong Choi[1], Jin Sub Choi[1], Myoung Soo Kim[1], Soon Il Kim[1], Soo Jin Kim[1], Hyung Soon Lee[3], Jung Jun Lee[4]
[1]Yonsei College Of Medicine/Severance Hospital, Korea; [2]Yonsei College Of Medicine/Gangnam Severance Hospital, Korea; [3]National Health Insurance Cooperation/Ilsan Hospital, Korea; [4]Cha University/Cha Bundang Medical Center, Korea

Background: Lactate clearance (LC) has been demonstrated as a prognostic factor of critically ill patients in many recent studies. Lowering blood lactate level is mainly associated with intact liver function, however, there are few studies concerning the relationship between LC and allograft function after liver transplantation. The aim of this study is to evaluate predictive value of LC for the development of early allograft dysfunction (EAD) and its clinical significance for short term outcome after liver transplantation.
Methods: We performed a retrospective analysis for 215 consecutive deceased donor liver transplantations from January 2011 to May 2016. Serial LCs were calculated within 6, 12, 18 and 24 h after reperfusion (LC6, LC12, LC18 and LC24).
Result: EAD was developed in 50 patients (25.8%). MELD score (18.9 ± 8.7 vs. 22.2 ± 10.2, p = 0.028), intraoperative transfusion (4150 ml, IQR 4950 vs. 5425 ml, IQR 9338, p = 0.045) were significantly higher and all measured LCs were significantly lower in EAD group.
In receiver operating characteristic (ROC) analysis, LC6 showed the highest area under curve (AUC) value of 0.846 (95% CI 0.782–0.911) to predict the development of EAD and its cut-off value was 25.8% with 79.6% sensitivity and 79.0% specificity.
When separated on the basis of each cut-off level, Low LCs demonstrated significant correlation with EAD in multivariate analysis and adjusted odds ratio (OR) of Low LC6 was the highest. (OR=18.159, 95% CI 7.231–45.599)
In-hospital mortality and 6 month mortality were higher in each Low LC group than High LC group with statistical significance for LC 6, 18, 24 and without statistical significance for LC 12.
Conclusion: LC shortly after reperfusion of allograft is significantly discriminative for the development of EAD and associated with short term prognosis in deceased donor liver transplantation.





Clinical Pancreas/Islet Surgical technique

BOS252 OUTCOMES OF PANCREAS TRANSPLANTATION WITH DUODENO-DUODENAL ENTEROSTOMY AND ENDOSCOPIC SURVEILLANCE

Jørn-Petter Lindahl, Rune Horneland, Espen Nordheim, Anders Hartmann, Einar Martin Aandahl, Krzysztof Grzyb, Håkon Haugaa, Gisle Kjøsen, Anders Åsberg, Trond Jenssen
Rikshospitalet, Ous, Norway

Background: Until recently pancreas transplantation has been performed with exocrine drainage via duodenojejunostomy. Since 2012, duodenojejunostomy was substituted with duodenoduodenostomy in our hospital, allowing endoscopic access for biopsies.
Methods: In this study we assessed (1) safety profiles with duodenoduodenostomy versus duodenojejunostomy procedures, and (2) graft rejection rate and graft loss with the duodenoduodenostomy technique in pancreas transplantation alone (PTA) compared with simultaneous pancreas and kidney (SPK) transplantation. Duodenoduodenostomy was performed in 117 patients (55 PTA and 62 SPK patients with a median follow-up of 2.2 years). The results were compared with 167 SPK duodenojejunostomy patients transplanted in the period 1998-2012 (pre-duodenoduodenostomy era).
Results: (1) Postoperative bleeding requiring reoperation occurred in 18% of duodenoduodenostomy patients versus 10% of duodenojejunostomy patients (p = 0.039). Occurrence of pancreas graft vein thrombosis was not different between the groups, 9% and 6% respectively (p = 0.20). (2) More patients with SPK-duodenoduodenostomy than PTA-duodenoduodenostomy patients were males (p = 0.016), had longer history of diabetes (p = 0.018) and more often coronary artery disease (p = 0.025). Pancreas graft rejection rates were higher in PTA-duodenoduodenostomy transplants versus SPK-duodenoduodenostomy patients (p = 0.003). Hazard ratio (HR) for graft loss was 2.25 (95% CI 1.00, 5.05; p = 0.049) in PTA-duodenoduodenostomy versus SPK-duodenoduodenostomy recipients.
Conclusions: (1) Patients who had a duodenoduodenostomy more often had bleeding requiring reoperation than duodenojejunostomy patients. (2) Pancreas transplantation alone patients with duodenoduodenostomy had more rejections and graft losses compared with patients with simultaneous kidney and pancreas transplantation with duodenoduodenostomy.

Clinical Pancreas/Islet Donation and donor types

BOS253 A SINGLE-CENTRE EXPERIENCE OF DONATION AFTER CARDIAC DEATH PANCREAS TRANSPLANTATION

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Background: The utilisation of pancreas allografts derived from controlled donation after cardiac death (DCD) donors has greatly expanded the organ pool in the United Kingdom in recent years. This study presents the largest single-centre experience of DCD pancreas transplantation to date. The aim of this study is to compare outcomes for pancreas allografts from DCD and donation after brain death (DBD) donors.
Methods: Retrospective single-centre analysis of all DCD and DBD pancreas transplants between March 2010 and March 2016 were reviewed. Donor and recipient characteristics were analysed. Primary endpoints were patient death, allograft failure, delayed graft function, primary non-function, length of stay and re-operation. Enteric drainage was established via Roux-en-y enteric anastomoses in all cases.
Results: SPK from 47 DCD and 84 DBD donors were carried out. Donor and recipient demographics were similar in both groups with mean cold ischaemic times for DCD of 633 (range, 362-806) and DBD of 599 (range, 286-823) (p = 0.17). The mean length of stay post transplant for DCD and DBD allografts were 25 and 22 days respectively (p = 0.656). Patient 1-year survival was

100% for DCD and 95% for DBD. Pancreas allograft survival rates were not significantly different with Kaplan-Meier 1-year graft survival estimates of 96 and 89 per cent for DCD and DBD respectively (p = 0.218).
Conclusions: Criteria DCD pancreas allografts have comparable outcomes to DBD allografts.

Clinical Pancreas/Islet Surgical technique

BOS254 PANCREAS TRANSPLANTATION: ADVANTAGES OF A RETROPERITONEAL GRAFT POSITION

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Hospital Clinic Barcelona, Spain

Background: We present our experience of a modified technique for transplant, with the pancreas placed into a fully retroperitoneal position with systemic venous and enteric drainage of the graft by duodeno-duodenostomy, in particular, focusing on postoperative complications.
Methods: All pancreas transplantations performed between May 2016 and January 2017 were prospectively entered into our transplant database and analyzed retrospectively.
Results: The retroperitoneal technique was used to transplant 10 pancreata. The pancreas was transplanted simultaneously with a kidney procured from the same cadaveric donor (n = 9). In one case the pancreas was transplanted after a kidney transplant from a living donor. The study group included 6 men and 4 women of median age of 41 years (36-54) and median pre-transplant diabetes type 1 duration of 29.50 years (19-44). Median cold ischemia times of the pancreas were 10.30 h (5.30–12.10). The preservation solution used was Celsior (n = 7), IGL-1 (n = 2), and UW (n = 1). No graft was lost due to the location of the graft. In one patient, a transplantectomy at 12 h was needed because of a graft thrombosis arising from a donor with prolonged cardio-respiratory arrest, and was probably related to ischemic conditions. The duodenostomy was closed without complications. Another procedure was aborted (i.e. without completing the graft implant) due to an intraoperative immediate arterial thrombosis in a patient with severe iliac atheromatosis. No graft was lost to portal thrombosis. The median hospital stay averaged 13.50 days (10–27). No primary pancreas non-function occurred in the remaining eight patients.
Conclusions: Retroperitoneal graft placement appears feasible and has advantages such as easy access for dissection the vascular site; comfortable and easy technical vascular reconstruction; and a decreased risk of intestinal obstruction by separation of the small bowel from the pancreas graft.

Clinical Pancreas/Islet Other

BOS255 SIXTEEN YEARS' EXPERIENCE ON PANCREAS-KIDNEY TRANSPLANTATION – SEARCHING FOR FACTORS LEADING TO BETTER RESULTS

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During the 16 activity years of our pancreas transplant program 198 SPKT were performed, with enteric diversion and vascular anastomosis to systemic circulation. We have analyzed global outcomes and we also compared results obtained from two periods: period 1 (2000–2008) and period 2 (2009–2016).

The global group of 198 SPKT, 50.5% female, aged 35 ± 6 years (y), had been on dialysis for 27 ± 20 months (m) and had 24 ± 6 years of diabetes evolution. Anti-lymphocyte globulin, tacrolimus, mycophenolate and steroids were used as induction therapy. The deceased donor (mainly traumatic) mean age was 28 ± 11 years. The median admission time was 18 days (d). Delayed kidney graft function (DGF) occurred in 13.1%; acute rejection (AR) in 14.1%; and surgical reinterventions were needed in 24.7%. Overall survival results at 1, 5 and 10 years were: 97%, 95% and 91% for the patient; 96%, 94% and 84% for the kidney; 88%, 81% and 76% for the pancreas, respectively.

Comparing SPKT results between period 1 and 2 we found significant differences in several indicators. Patients were older in period 2 (36 ± 6 years vs. 34 ± 6 years, p = 0.014) and had a shorter time on dialysis (22 ± 14 vs. 33 ± 25 months, p = 0.001). They had a shorter admission length (20 ± 15 vs. 29 ± 21 days, p < 0.001). In period 2, DGF rate was lower (7.3% vs. 20.5%, p = 0.006); and surgical reinterventions per patient were less frequent (0.25 ± 0.87 vs. 0.72 ± 1.58, p = 0.014). Pancreas graft survival increased at 1 and 5 years from 80% and 76% in period 1 to 92% and 87% in period 2, which was almost statistically significant (p = 0.054). Patient and kidney graft survival were similar in the two periods.

Conclusions: SPKT outcomes have improved overtime, similarly to the most recent international results. Time on dialysis before SPKT diminished, a reflex of an earlier referral and of a better program response. Despite the higher patients' age in period 2, better pancreas outcomes and lower rates of reinterventions and DGF are the expression of a successful learning curve of our SPKT program.

Clinical Pancreas/Islet Donation and donor types

BOS256 PREPROCUREMENT PANCREAS SUITABILITY SCORE AND DONOR AGE/BMI-BASED MODEL BUT NOT PANCREAS DONOR RISK INDEX PREDICT PANCREAS GRAFT SURVIVAL

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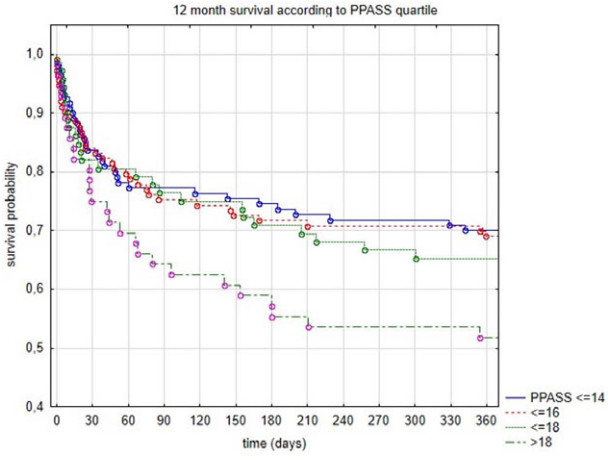
Preprocurement pancreas suitability score (PPASS) and Pancreas Donor Risk Index (PDRI) are two methods of objective assessment of pancreas donors. Poltransplant uses PPASS while PDRI is not considered. Most of European centers predict risk of organ loss with PDRI. The aim of the study was to validate applicability of PDRI and PPASS in Polish population.
Methods: Since February 1998 till September 2015, in all four active centers in Poland, 408 pancreas transplantations were performed: 366 (89.8%) simultaneous pancreas kidney and 42 (10.2%) pancreas transplants alone or pancreas after kidney. In recipients with available 12 month follow-up PPASS could have been calculated for 355 donors, PDRI for 252 (in 232 donors both indices could have been calculated). The end point of this research was death uncensored twelve months graft survival.
Results: One-year pancreas graft survival was 67.7%. PDRI did not predict graft loss. Univariate Cox analysis showed donor age (HR 1.039), BMI (HR 1.059) and PPASS (HR 1.089) to be significant risk factors for graft loss at 12 months. Risk model based on PPASS area under the ROC curve was 0.589 (CI 0.539–0.637) and was not superior to a donor age/BMI-based model (area under ROC curve 0.61, CI 0.56–0.658, test accuracy 72.7%). PPASS >17 was associated with risk of pancreatic graft loss (accuracy 65.5%). Twelve-month survival curves according to PPASS quartile are shown on a figure.
Conclusion: PDRI does not predict pancreas graft function at 12 months following transplantation. PPASS and especially donor age/BMI model performed much better in Polish population.



Clinical Pancreas/Islet Rejection

BOS257 DECLINE IN PANCREAS TRANSPLANT INCIDENCE DESPITE AN IMPROVEMENT IN PATIENT AND GRAFT SURVIVALS: LONG-TERM FOLLOW-UP IN A LARGE VOLUME CENTER

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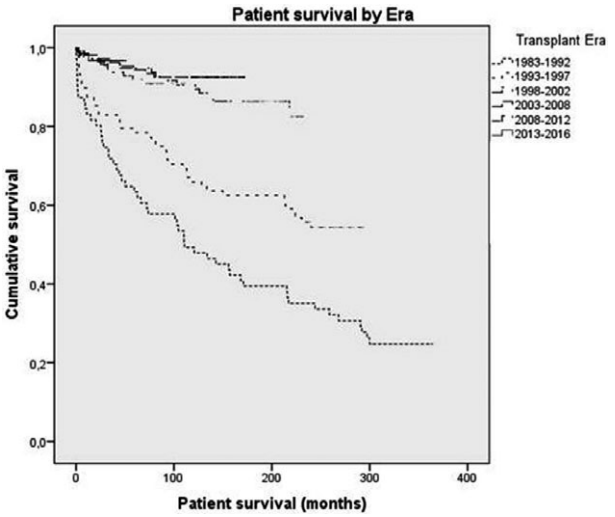
Background: Pancreas transplantation is the best treatment option for selected type 1 diabetic patients with end-stage renal disease, but a decline in total number of transplants has been felt in western countries, with some emphasis in the lack of involvement from low-volume centers.
Methods: We evaluated all pancreas transplants performed at our center since February 4, 1983 to December 31, 2016. Transplant eras were defined as the first decade (1983–1992), and thereafter 5 year intervals. Donor, recipient, transplant, and immunosuppression data were included. Univariate and multivariate analysis were performed for all parameters, Kaplan-Mayer for patient and graft survivals, and Cox-regression models designed for death and graft failure risk.
Results: A total of 542 pancreas transplants were performed, including 57 PAK and 9 PTA. In the first era 73% received horse antilymphocyte serum as induction therapy, 77% OKT3 in the second, 49% anti-thymocyte globulin in the 3rd, over 70% basiliximab from 2003–2012, and currently 92% receive thymoglobulin. Urinary exocrine drainage was performed until 1995, with enteric drainage performed in almost every transplant afterwards.

One year death-censured graft survival improved from 49% in the first era to the current 85% ($p = 0.000$), and at 5-years doubled from 40% to 81% ($p = 0.000$) (Figure 1). In last decade, an 89% five-year graft survival was found when excluded the first 90 days post-transplant. Ten-year patient survival increased from 49% to 90% ($p = 0.000$). Both donor and recipient age increased during this period ($p < 0.005$), without differences in BMI. Despite these results, in the last 7 years there is a steady decline in the number of transplants (20%–30%).
Conclusions: This study highlights the significant increase in graft and patient survival in pancreas transplant recipients in a large volume center. Nonetheless further analyses are warranted to identify the reasons for the steady decrease in the number of transplants.



Clinical Pancreas/Islet Surgical technique

BOS258 EN BLOC SIMULTANEOUS PANCREAS AND KIDNEY COMPOSITE GRAFT TRANSPLANT WITH LIMITED VASCULAR ACCESS

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Purpose: Limited vascular access could be encountered in an obese or re-transplant patient. We described modifications that facilitated an en bloc simultaneous pancreas and kidney (SPK) composite graft transplant in 4 diabetic patients with renal failure under hemodialysis.
Materials and Methods: At the back-table, the superior mesenteric artery and splenic artery of the pancreas graft were reconstructed with a long "Y" iliac artery graft. The smaller left renal artery is anastomosed end-to-side to the larger and longer common limb of the arterial Y graft and the shorter portal vein is anastomosed end-to-side to the longer graft left renal vein. Thus, this en bloc composite graft allowed to facilitate "real" SPK transplant using single common graft artery and vein for anastomosis to one recipient arterial and venous site. The en bloc pancreas and kidney composite graft was implanted by suturing the graft left renal vein to IVC and graft common iliac artery the recipient distal aorta. Exocrine drainage was provided by anastomosis of the graft duodenum to a roux-en-y jejunum limb in a side-to-side fashion. Immunosuppressants included basiliximab, tacrolimus, mycophenolate mofetil, and methylprednisolone.
Results: The mean operative time was 7 h with mean cold ischemic time of 6 h and mean warm ischemic time of 47 min. The mean hospital stay was 20 days, with a serum creatinine level of 1.4 ng/ml and a blood glucose level of 121 mg/dl. There was no rejection episode or postoperative complication after the en bloc SPK transplant.
Conclusion: En bloc pancreas and kidney composite graft might be an option for patients with limited vascular access. This technique (1) facilitates "real" simultaneous pancreas and kidney (SPK) transplant with only single common artery and vein for implanting the composite graft; (2) minimizes dissection of vessels and conserves recipient vessels.

BOS259 PANCREAS TRANSPLANT AT TAIPEI VETERANS GENERAL HOSPITAL

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Type 1 diabetes eventually leads to nephropathy, neuropathy, retinopathy and angiopathy after 10–30 years. Currently, pancreas transplant is the treatment of choice in tight control of blood sugar for IDDM patients, and further to stabilize, prevent or even to reverse the diabetic complications. We will present our experience in pancreas transplant which was initiated on September 19, 2003. From September 2003 to October. 2016, there were 133 pancreas transplants performed for 128 patients at Taipei Veterans General Hospital, with 36 SPK, 16 PAK, 62 PTA, 19 PBK and 1 PAL (pancreas after liver transplant). Most (78.5%) of our pancreas transplants were for IDDM patients. The blood sugar usually returned to normal level within 5 h (median) after revascularization of the pancreas grafts. The fasting blood sugar maintained within normal range thereafter throughout the whole clinical course in most cases. There were 2 surgical mortalities. The technical success rate was 96.5%. Excluding the 4 cases with technique failure, overall 1-year pancreas graft survival is 98.5% and 5-year is 94.1%, with 100% 1-year for SPK, 97.1% 1-year for PTA, 100% 1-year for PAK and 100% 1-year for PBK.

In conclusion, pancreas transplant provided an ideal insulin-free solution for DM, especially IDDM. Pancreas transplant could be performed with similar successful rate irrespective of the type of pancreas transplant at our hospital.

Clinical Pancreas/Islet Donation and donor types

BOS260 SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION FROM DONORS AFTER BRAIN DEATH (DBD) AND DONORS AFTER CARDIAC DEATH (DCD): A 30-YEAR FOLLOW-UP STUDY AT KAROLINSKA UNIVERSITY HOSPITAL

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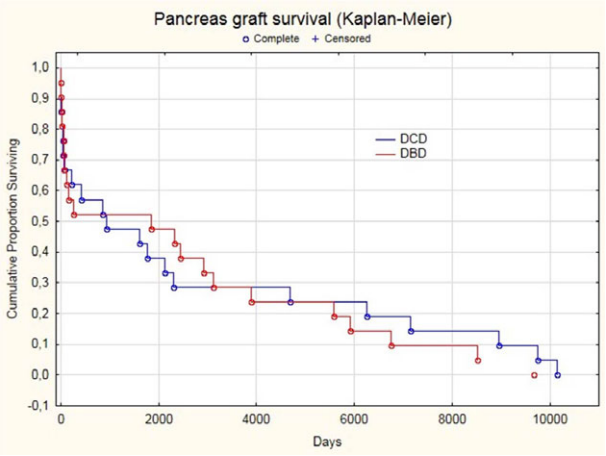
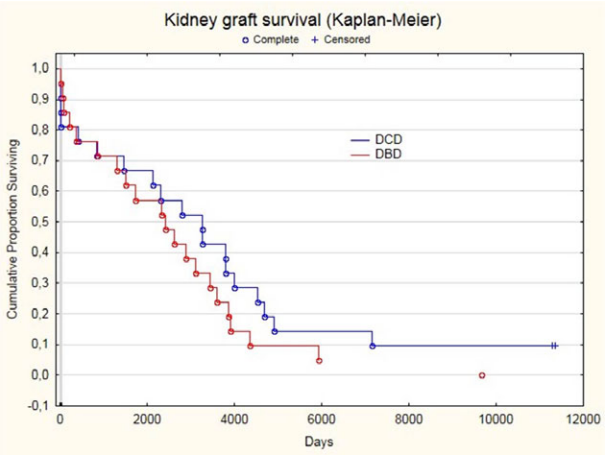
Background: Although the use of DBD has led to a higher number of pancreas transplantations over the last decade in Scandiatransplant, an imbalance between demand and availability of transplantable organs still

persists. This has led to a debate on reintroducing DCD – the standard donor in Sweden before January 1988.
Methods/Materials: We analyzed 44 consecutive simultaneous pancreas kidney transplant (SPK-tx) patients, 21 received DCD grafts during 1986–87 and 23 received DBD grafts during 1988–91 at Karolinska University Hospital.
Results: Warm ischemia time (WIT) was very short in the DCD group (which could be due to DCD being controlled Maastricht category IV). Pancreas and kidney cold ischemia time (CIT) was significantly longer in the DBD group. Other significant differences were the use of segmental or whole graft and the use of arterial Y graft (Table 1). Graft and patient survival were similar for both groups (Figures 1 and 2).
Conclusion: This 30-year follow-up suggests that controlled DCD pancreas grafts with short WIT can be a feasible option to reduce organ shortage without negative impact on the long terms results.

	DCD (21 pat)	DBD (23 pat)	p value
R – Age (years)	37 ± 5.5	35 ± 7.1	NS
R – Gender (F-M)	10–11	10–13	NS
R – BMI	21.5 ± 1.6	22.4 ± 2.6	NS
Duration of disease (years)	26 ± 6.2	24 ± 7.5	NS
Pretransplant dialysis	9 (43%)	12 (52%)	NS
D – Age	37 ± 16.2	35 ± 11.5	NS
D – Gender (F-M)	6–5	10–13	NS
D – BMI	22.7 ± 3.2 (M 10)	24.2 ± 4 (M 2)	NS
D – Cause of death			
Intracranial bleeding/stroke	13	14	
Brain trauma	4	6	
Asphyxiation	3	1	
Cardiovascular	1	1	
Other	0	1	
D – Creatinine	104 ± 33 (M 1)	92 ± 41 (M 1)	NS
D – Amylase	4 ± 3.1	6 ± 6.0	NS
D – Glucose	12 ± 6.2	9 ± 3.8	NS
CMV mismatch	2 (13%) (M 6)	9 (39%)	NS
Type of pancreas graft (segmental – whole)	21–0	2–21	<0.001
Arterial Y graft	0	7 (30%)	0.006
Interposition vein graft	0	2 (9%)	NS
Temporary pancreas catheter	21 (100%)	20 (87%)	NS
WIT (min)	4 ± 4.5	–	
CIT pancreas (min)	263 ± 56	375 ± 166	0.005
CIT kidney (min)	566 ± 117	715 ± 183	0.003
Immunosuppression			
CAP	7 (33%)	10 (43%)	NS
CAP + induction (ATG or OKT3)	14 (67%)	13 (57%)	NS
DGF pancreas	6 (29%)	10 (43%)	NS
DGF kidney	4 (19%)	1 (4%)	NS
Retransplant pancreas	1 (5%)	1 (4%) (M 3)	NS
Retransplant kidney	5 (24%)	4 (20%) (M 3)	NS

NS not significant, R recipient, F female, M male, D donor, CAP cyclosporine-azathioprine-prednisolone, DGF delayed graft function, M missing patients.





Clinical Pancreas/Islet Histology

BOS261

DOES DUODENO- DUODENAL ANASTOMOSIS OF PANCREAS TRANSPLANTS ALLOWS FOR REPRESENTATIVE ENDOSCOPIC ULTRASOUND-GUIDED BIOPSIES?

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Background: To assess whether a surgical technique with duodeno- duodenal anastomosis of pancreas transplants (PTX) allows for representative endoscopic ultrasound- guided biopsies.
Methods: Most centers implant pancreas grafts using enteric drainage as surgical technique. To facilitate endoscopic access for PTXs biopsies our center changed from the duodeno-jejunal anastomosis to the duodeno-duodenal anastomosis in September 2012. We evaluate the results from endoscopic ultrasound- guided biopsies (EUS) sampled from September 2012 to November 2016, and compared them with the results from ultrasound-guided percutaneous biopsies (PC) in the same time period.
Results: The study included 212 EUS and 96 PC from 103 PTX recipients. Overall EUS yielded tissue samples representative for BANFF classification in 50% of the cases, significantly lower than the 77% obtained with PC samples ($p < 0.05$). However, the success rate for EUS increased continuously during the study period, and during the last year 73% of the EUS protocol biopsies ($n = 36$) were representative and comparable to PC samples. Six patients had some temporary increase in plasma amylase after EUS but no severe complications were registered. One patient developed life- threatening bleeding from the pancreas graft after transcutaneous pancreas graft biopsy sampling.
Conclusions/interpretation: With some experience EUS is an efficient and safe way to harvest PTX biopsies.

Clinical Pancreas/Islet Cardiovascular complications

BOS262 COMPARISON OF DIFFERENT MARKERS OF VASCULAR DAMAGE IN TYPE 1 DIABETIC PATIENTS WITH END-STAGE RENAL DISEASE AFTER SPK OR KTX

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Background: Normalized glucose metabolism is expected to lead to remodeling of arterial walls in patients with end-stage renal disease (ESRD) caused by type 1 diabetes (T1D) after simultaneous pancreas-kidney transplantation (SPK) compared to patients after kidney transplantation (KTx).

The aim of the study was to compare the severity of vascular damage based on imaging methods, functional tests, and biochemical measurements in patients with ESRD caused by T1D after SPK or KTx in follow-up period after transplantation.

Methods/Materials: 39 SPK, 39 T1D KTx, and 52 non-diabetic KTx recipients were enrolled into the study. In all participants intima-media thickness (IMT) and pulse wave velocity (PWV) were measured, and glycated haemoglobin (HbA_{1C}), creatinine, lipids, osteoprotegerin (OPG), matrix metallopeptidase-9 (MMP-9), and fetuin A were assessed in blood, serum, or plasma.

Results: During 58 $\pm$ 31 months follow-up period, SPK but not KTx resulted in normalization of HbA_{1C}. Serum triglycerides levels were lower in SPK than in T1D KTx group (0.95 $\pm$ 0.65 vs. 1.42 $\pm$ 0.49, $p < 0.01$ mmol/l), but concentrations of cholesterol and its fractions were similar. Estimated glomerular filtration rate (eGFR) was greater in SPK than in T1D KTx group (71.8 $\pm$ 27.6 vs. 52.0 $\pm$ 23.8 ml/min; $p < 0.01$). IMT in SPK was lower than in T1D KTx (0.64 $\pm$ 0.13 vs. 0.74 $\pm$ 0.13 mm, $p < 0.01$), but PWV values and OPG, MMP-9, and fetuin A levels did not differ between analyzed groups.

In the group of diabetic SPK or KTx recipients IMT was associated with HbA_{1C} ($\beta = 0.479$), total cholesterol ($\beta = 0.045$), triglycerides ($\beta = 0.071$), MMP-9 ($\beta = 0.039$), and inversely with eGFR ($\beta = -0.014$, in all $p < 0.01$).

Conclusions: Normalized glucose metabolism, improved serum lipids profile and better kidney graft function seem to slow the progression of atherosclerosis, but without improvement in arterial stiffness in patients with ESRD caused by T1D after SPK compared to KTx.

Clinical Pancreas/Islet Allocation

BOS263 DEVELOPMENT AND VALIDATION OF A PROGNOSTIC MODEL FOR KIDNEY FUNCTION ONE YEAR AFTER COMBINED PANCREAS AND KIDNEY TRANSPLANTATION

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Background: The widening gap between demand and supply of organs for transplantation provides extraordinary challenges for ethical donor organ allocation rules including the balancing of urgency and utility. The aim of this study is the development of a prognostic model for the prediction of kidney function 1 year after simultaneous pancreas and kidney transplantation (PKTx).

Methods: Included were patients with end-stage renal failure due to diabetic nephropathy. Multivariable logistic regression modelling was applied for prognostic model design with retrospective data from Hannover Medical School, Germany, followed by prospective internal and retrospective external validation from data of the transplant center in Kiel, Germany. Retrospective data from another German transplant center in Kiel was retrieved for external model validation via the initially derived logit link function. Receiver operating characteristic (ROC) curve analysis was performed to assess the model's clinical applicability.

Results: Recipient model: $y_1 = 8.269 - 0.200 * \text{age} - 0.410 * \text{time from diabetes diagnosis until PKTx in years} + \text{diabetic retinopathy if yes} = 0.999, \text{if no} = -0.999 + \text{male if yes} = 0.757, \text{if no} = -0.757 + 0.010 * (\text{age} * \text{time from diabetes diagnosis until PKTx in years})$

Donor Model: $y_2 = 0.873 + \text{male if yes} = -1.812, \text{if no} = 1.812 + 0.065 * \text{age} - 1.479$*

Meta model: $y_3 = -1.329 + 1.335 * \text{Logit } y_1 + 1.098 * \text{Logit } y_2$

The developed prognostic model is able to predict kidney graft function one year after transplantation $\geq$ KDIGO stage III with high areas under the ROC-curve in the development cohort (0.943) as well as the internal (0.807) and external validation cohorts (0.784).

Conclusion: The proposed validated model is a valuable tool to optimize present allocation rules with the goal to prevent transplant futility. It might be used to support donor organ acceptance decisions for individual recipients.

Clinical Pancreas/Islet Other

BOS264 PANCREAS RETRANSPLANTATION IS NOT ASSOCIATED WITH POOR GRAFT SURVIVAL AND COULD BE CONSIDERED FOR SELECTED PATIENTS WITH PRIMARY PANCREATIC ALLOGRAFT FAILURE

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Background: Pancreas transplantation is one of the best treatment options for patients suffering from severe diabetes. However, a significant number of grafts are lost for technical and immunological reasons. Re-transplantation procedures are associated with increased rates of technical failure and rejection compared to the first ones. Pancreas re-transplantation is a real technical challenge due to adhesions from the first transplant and vascular difficulties. Just few data describing the results of pancreas re-transplantation, thereby outcomes are known thanks to registry data. The first studies about pancreas re-transplantation were associated with poor results. We report a large single center study of patients with pancreas re-transplantation. The aim of this study is to analyze the second pancreas transplantation results.

Materials/Methods: All pancreas re-transplantation that occurred in our single center were included. Graft survival, causes of graft loss and patients survival were analyzed.

Results: From January 1987 to February 2017, 540 pancreas transplantations were performed in our single center. 38 (7%) of this 540 pancreas transplantations were second transplantations. There was 9 female and 29 male, with a mean age of 42 years.

Graft survival was 64.5% at 5 years and 44.8% at 10 years (figure 1). 11 patients (28.9%) lost their second pancreas (3 from venous thrombosis, 2 from chronic rejection).

Patients survival was 85.2% at 5 years, 74% at 10 years (figure 2). Only one death was pancreas related (gas gangrene).

As for the kidney transplant, 5 patients had to go back on dialysis (4 for chronic kidney rejection, one after immunosuppressors arrest).

Conclusion: Second pancreas transplantation is no longer associated with poor graft survival and could be considered for selected patients with primary pancreatic allograft failure.

BOS265 PANCREAS AND KIDNEY GRAFT SURVIVAL IN RECIPIENTS OLDER THAN 60 YEAR AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION

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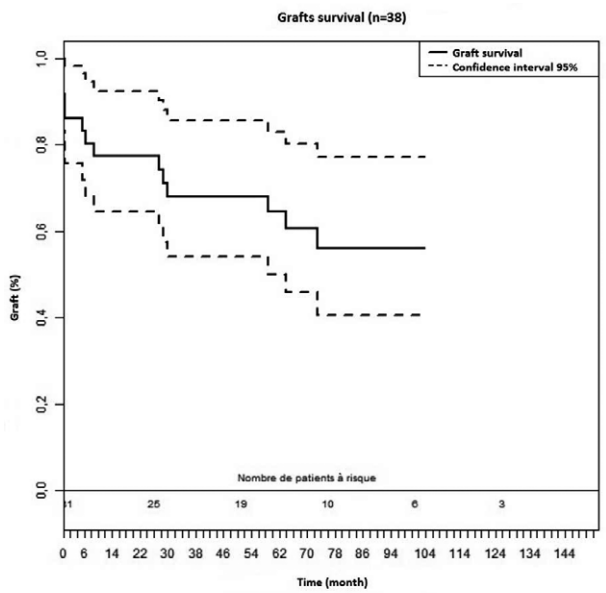
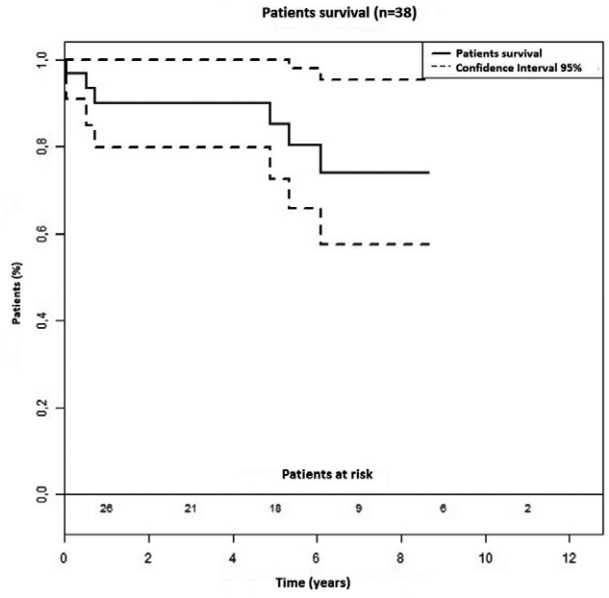
Introduction: Simultaneous pancreas and kidney transplantation (SPKTx) is rarely indicated in older recipients. The aim of this study was to retrospectively evaluate survival of the patients older than 60 years.

Methods: The retrospective analysis included patients with Type 1 diabetes mellitus who underwent 1. SPKTx in our center since 2000 to December 2016 ($n = 397$). The recipients were divided into the three groups according to the age; Group A (older than 60 year, $n = 21$), Group B (40-59y, $n = 211$) and Group C ($n = 170$, younger than 40 year). Kidney graft failure was defined as death, explantation, return to dialysis or kidney retransplantation. Pancreas graft failure was defined as death, graftectomy or return to permanent intensified insulin regimen. Survival curves were plotted using the Kaplan-Meier method and differences between curves were compared using the Cox-Mantel test.





Results: Cumulative patient survival after 10 years in Group A was 67%, which was significantly lower in comparison to Group C (90%, p = 0.005) but not Group B (88%, ns). Cardiovascular complications were the most common reason resulting in death (5, 5.6 and 2.9% in Groups A, B, and C, respectively), followed by infection or sepsis (9.5, 2.3 and 2.9% in Groups A, B, C.) Malignancy was reported in 2, 5 and 1 patients in Groups A, B and C, respectively. We have not found difference in pancreas graft survival among groups; Group A 62%, Group B 68%, Group C 66%, ns). Likewise, kidney grafts survival was similar; 62, 62 and 67% in Groups A, B and C, respectively (ns). In Group A 1 kidney graft failed due to fibrosis and 1 pancreas was explanted due to bleeding. The non-immune reasons were the most frequent cause of the pancreas failure (8% in Group B 11% in Group C, ns). Twelve and 8 kidney grafts in Group B and C failed due to rejection (ns).
Conclusion: Overall pancreas and kidney grafts survivals were comparable among the groups. Neither pancreas nor kidney grafts were lost due to rejection in older individuals.

Clinical Kidney Rejection

BOS266 IS THERE A NEED FOR A SUPPLEMENTARY DOSE OF ECULIZUMAB AFTER ANTIBODY REMOVAL FOR TREATMENT OF ANTIBODY-MEDIATED REJECTION?

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Background: Antibodies directed against either ABO blood group or HLA antigens can damage endothelial cells in the renal allograft by activation of the complement cascade. Eculizumab inhibits complement protein C5 preventing formation of the membrane attack complex and is being increasingly used in the treatment of antibody-mediated rejection (AMR) in combination with antibody removal. A supplementary dose of eculizumab is recommended after each plasma exchange procedure to ensure a therapeutic concentration. There are no studies evaluating the need for eculizumab replacement after double filtration plasmapheresis (DFPP) and immunoadsorption (IA).
Methods: We have measured levels of eculizumab before and after DFPP and Therasorb IA in a patient treated for antibody-mediated rejection. Drug levels over time were calculated using the formula $C1 = C0 * e^{(-\log/T * t)}$, where C1 = concentration after time *t*, C0 = initial concentration, *T* = half-life.
Results: Eculizumab concentration decreased from 265.3 μg/ml to 114.8 μg/ml after DFPP and from 168.7 μg/ml to 109.9 μg/ml after Therasorb IA (43.7% and 65.1% of the concentration prior to antibody removal procedure, respectively). Taking into consideration the half-life of eculizumab (on average 261–271 hours), in both cases a concentration higher than 50 μg/ml (recommended concentration in the treatment of aHUS) would persist for 12 days (313–325 and 297–308 hours respectively). A supplementary dose of 600 mg was given in both cases with peak levels after 1 hour of infusion of 347.9 μg/ml and 257.2 μg/ml respectively. A concentration higher than 50 μg/ml would last for at least 26 days (730–758 and 617–649 hours respectively).
Conclusions: Even though eculizumab concentration decreases during DFPP and Therasorb IA, a supplementary dose is probably not necessary after a single antibody removal procedure. It should be consider if two or more antibody removal sessions are required.

BOS267 DSA PRESENCE DOES NOT AFFECT RENAL HISTOLOGY AND CLINICAL OUTCOME IN CHRONIC ACTIVE ANTIBODY MEDIATED REJECTION

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Background: Chronic active antibody mediated rejection (caABMR) is a major cause of long term renal allograft dysfunction. It is defined by the presence of microvascular inflammation, histopathological changes compatible with transplant glomerulopathy (TG) and the presence of donor specific antibodies (DSA).

Although considered mandatory for the diagnosis of caABMR, it is not uncommon for caABMR to present itself without detectable DSA. In this study we evaluated whether the presence of DSA is associated with a different renal histology, allograft survival and response to therapy.
Methods: Forty-one biopsy-proven caABMR patients were included retrospectively. All patients had progressive loss of allograft function and were treated similarly after diagnosis regardless of DSA status. DSA status was determined by the single bead Luminex assay. The clinical characteristics, histomorphology, renal allograft function, response to therapy and survival were compared between the DSA+ ($N = 17$) and DSA− ($N = 24$) patients.
Results: There were no statistically significant differences found in the clinical characteristics, renal allograft survival and histomorphologic lesions between both patient groups. Both groups showed substantial and severe chronic histomorphological damage and inflammation, consistent with caABMR. Decline in allograft function was similar without a significant difference in treatment effect between the two groups (p = 0.93).

However, DSA+ patients with C4d positive staining in the peritubular capillaries showed a significantly steeper decline in allograft function prior to caABMR diagnosis, along with a significantly better response to therapy compared to C4d− DSA+ patients (p = 0.01).
Conclusion: The presence or absence of detectable DSA has no significant association with renal histology and clinical outcome in caABMR patients, except for the subgroup of C4d+DSA+ cases which respond better to therapy.

Translational Kidney Rejection

BOS268 PERIPHERAL LEUKOCYTE PROFILES IN LATE ANTIBODY MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Antibody-mediated rejection (ABMR) is one of the major causes of late kidney allograft dysfunction and loss. Complement-dependent and -independent pathomechanisms, which may involve a variety of cellular components, were suggested to promote tissue inflammation and injury. Focusing on subclinical late ABMR, we here investigated whether ongoing rejection is associated with changes in peripheral blood leukocyte subsets.

This study included 144 long-term stable kidney transplant recipients (eGFR >20 ml/min/1.73 m^2, median time after transplantation: 5.5 years, IQR 2.7–13.1), whereas 45 recipients were ABMR positive and 99 ABMR negative.

A higher number of transitional B cells [CD19 + CD45 ++CD10 + CD27-CD38 ++; median 0.8% vs. 0.2% of total B cells, p = 0.03; absolute counts, median: 0.7 (IQR 0.1–2.5) vs. 0.2 (IQR 0.0–0.9), p = 0.02], less CD14+ monocytes [median 7% vs. 8% of total leukocytes, p = 0.004; absolute counts, median: 500 (IQR 408–565) vs. 608 (IQR 474–760), p < 0.001) and less CD4+ T cells (CD3+ CD4+ ; median 52% vs. 58% of total T cells, p = 0.006; absolute counts, mean: 448 (IQR 220–779) vs. 647 (IQR 501–864), p = 0.001) were detected in the peripheral blood of DSA+ABMR+ as compared to DSA-ABMR-patients. Differences remained significant in multivariate models (relative counts; transitional B cells: OR 1.40, CI 0.90–2.22; monocytes: OR 0.87, CI 0.76–0.99; CD4+ T cells: OR 0.19, CI 0.003–1.20). There were no significant differences regarding granulocytes, CD16+ CD56+ NK cells, CD8+ T cells (CD3+ CD8+), naïve (CD19+ CD45++ CD10– CD27– CD38+) and memory B cells (CD19+ CD45++ CD10– CD27+ CD38+) or plasma cells (CD19+ CD45++ CD10-CD27++ CD38+++), respectively.

The results of this study revealed that ongoing ABMR late after transplantation associated with subtle changes of distinct peripheral blood leukocyte subsets, including T cells, B cells and monocytes. Our data suggest that the assessment of changes in leukocyte profiles may help dissect the quality of an ongoing alloimmune process.

Clinical Kidney Immunology

BOS269 DE NOVO DONOR-SPECIFIC HLA ANTIBODIES AFTER STEROID WITHDRAWAL IN KIDNEY TRANSPLANT RECIPIENTS: A PROSPECTIVE, RANDOMIZED, CONTROLLED, PARALLEL GROUP STUDY. PRELIMINARY RESULTS

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Introduction: Steroids represent one of the mainstays of immunosuppression after kidney transplant (KT). Steroid withdrawal reduces metabolic and cardiovascular complications, but whether it increases the risk of acute rejection and the generation of donor-specific anti-HLA antibodies (DSA) is currently undetermined.
Material and methods: In a controlled clinical trial (NCT02284464), a total of 176 KT patients with low immunological risk were recruited to randomly receive either conventional triple immunosuppression: steroids, TAC and MMF versus steroid withdrawal at the third post-KT month. We compared the incidence of de novo DSA, determined by Luminex Mixed and Luminex Single Antigen (One Lambda®), and its impact on graft histology in patients with steroid withdrawal at the 3 post-KT month (after a protocol biopsy) versus patients who continue to receive conventional triple immunosuppression.
Results: So far, 68 patients have been randomized (34 per group), with no significant differences in the clinical and demographic characteristics between the groups. The intermediate analysis in those patients who had completed one year of follow-up (n = 28) showed no significant differences in the formation of DSA (0% vs. 0%), nor was there rejection in those patients in whom prednisone was withdrawn after randomization. Patients with triple therapy showed a trend toward better renal function compared to those without steroids at the first post-KT year (1.29 ± 0.25 vs. 1.56 ± 0.42 mg/dl, p = 0.088). HbA1c levels were similar between both group at the first post-KT year (5.79 ± 0.59 vs. 5.68 ± 0.81%, p = 0.734).
Conclusion: The preliminary results show that steroid withdrawal at the 3 month post-KT seems safe when assessing the appearance of rejection and formation of DSA compared to the patients who continued to receive conventional triple immunosuppression.

Clinical Kidney Rejection

BOS270 A LOWER MEAN EXPOSURE TO TACROLIMUS, NOT INTRA-PATIENT VARIABILITY IS ASSOCIATED WITH CHRONIC ACTIVE ANTIBODY MEDIATED REJECTION

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Background: Chronic active antibody mediated rejection (caABMR) is a major cause of long-term kidney graft loss. It is hypothesized that frequent underexposure and suboptimal trough levels of immunosuppressive drugs, in particular CNI, are risk factors for the development of caABMR.

The intra-patient variability (IPV) may serve as a substitute parameter for frequent underexposure and/or non-adherence. In this study we investigated the association between tacrolimus exposure and the development of caABMR.
Methods/Materials: We retrospectively included 59 *biopsy proven* caABMR patients and compared them to 189 matched controls. Controls were matched for age, year of transplantation and type of kidney donor. All patients were on a standard regimen of tacrolimus and MMF. The IPV was calculated from pre-dose tacrolimus concentrations measured in the 3 years prior to caABMR diagnosis. The IPV for the matched controls was measured over a similar period of time dependent on the case's time to caABMR diagnosis. Furthermore mean tacrolimus trough levels and renal allograft function were compared between both groups.
Results: The median time to caABMR diagnosis was 6 years [range 2–14 years]. The tacrolimus IPV was relatively high in both groups with 24.4% [range 12.0%–48.3%] for the cases versus 23.5% [range 7.9%–46.3%] for the controls (p = 0.40). The difference in mean tacrolimus concentration of 5.8 ng/ml for the cases and 6.1 ng/ml for the controls was nearly significant (p = 0.06).

There was, however, a statistically significant decline in both mean trough levels and allograft function over the 3 years for the cases. This declining trend was significantly different compared to the relatively stable trough levels and allograft functions of the controls (p = 0.03 and p < 0.001).
Conclusion: A lower mean exposure to tacrolimus but not a high intra-patient variability might contribute to the development of caABMR.

BOS271 PREDICTIVE VALUE OF RENAL POLY (ADP-RIBOSE) POLYMERASE (PARP) EXPRESSION BOTH IN INFLAMMATION AND INTERSTITIAL FIBROSIS PROCESSES IN RECIPIENTS WITH ANTIBODY-MEDIATED REJECTION

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Background: PARP is well considered to play an augmenting role in inflammation. However, its role in the development of fibrosis is not well defined. The aim of this study was to investigate the role of PARP both in inflammation and interstitial fibrosis (IF) processes in recipients with antibody-mediated rejection (AMR).
Methods: Among 100 patients 54 had pure AMR (Group 1) while 46 had both AMR and vascular rejection (Group 2). PARP, α-SMA, TNF-α, TGF-β and HLA-DR expression of tubules studied. Inflammatory cells in the peritubular capillaries (PTCs) and interstitium highlighted with PARP, TNF-α, HLA-DR, and CD68.
Results: Group 2 showed higher degrees of tubular PARP, α-SMA, TNF-α, TGF-β, and HLA-DR expression compared to Group 1 (p < 0.01). PARP, TNF-α and HLA-DR positive infiltrated cells and macrophage infiltration both in interstitium and PTCs found to be higher in Group 2 compared to Group 1 (p < 0.001). The extensity of PTC C4d expression increased with increasing degree of leukocyte infiltration both in PTCs and interstitium (p < 0.001). The time of the development of IF decreased with increasing intensity of PTC and interstitial leukocyte and macrophage infiltration (p < 0.001). Also, the development of IF shortened with increasing PARP, HLA-DR, TNF-α expression in inflammatory cells and increasing PARP, α-SMA, TNF-α, TGF-β, HLA-DR expression in tubular cells (P < 0.01). PARP expression on both tubules and infiltrated inflammatory cells showed poor graft outcome. The 5-year graft survival was 96% for recipients with negative tubular PARP while it was 18% for grade 3 tubular PARP expression respectively (p < 0.001).
Conclusion: Increased PARP activation leads to early graft loss with augmenting inflammation and interstitial fibrosis via activation of inflammatory signaling pathways and myofibroblastic differentiation of tubular cells. Therefore we suggest that PARP inhibitor drugs can combine with

Immunosuppressive therapy to control both inflammation and fibrosis Clinical Kidney Immunology

BD05272 DELETERIOUS EFFECT OF ANTI-ANGIOTENSIN II TYPE 1 RECEPTOR AND DONOR-SPECIFIC ANTI-HLA ANTIBODIES ON KIDNEY GRAFT OUTCOMES IS BOTH PROPER AND SYNERGISTICAL

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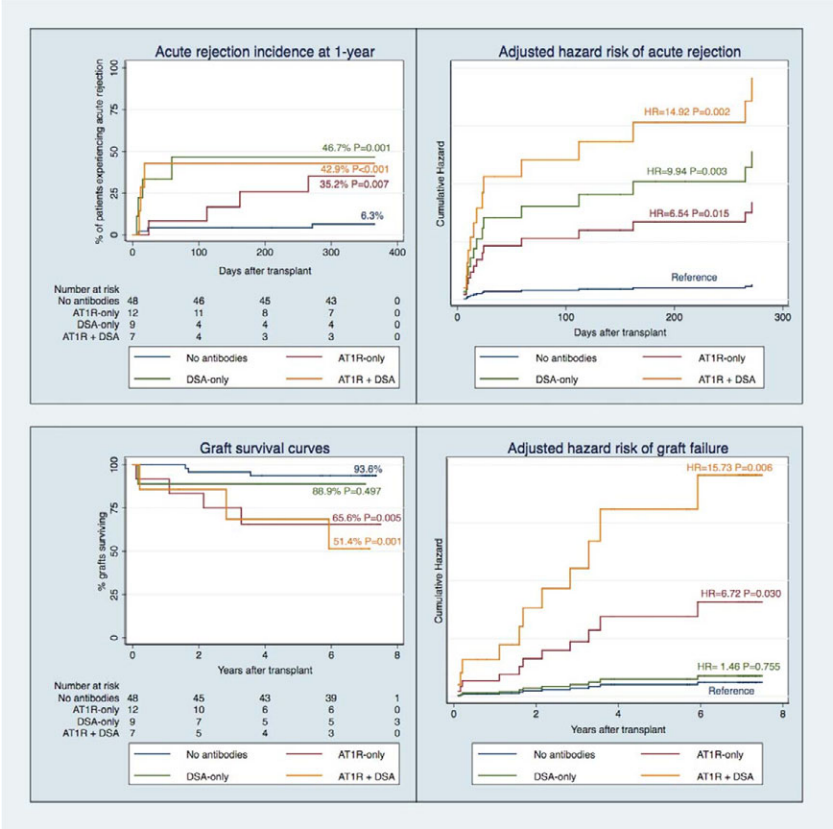
Background: Both DSA and AT1R antibodies have been associated with poor graft outcomes after kidney transplantation (KT), but their possible synergistic effect has been scarcely studied.
Methods: Seventy-six patients were randomly selected from our centre cohort of KT recipients for this exploratory study. DSA (MFI > 1000) and/or AT1R (>10 UI) were detected by solid-phase assays in pre-KT sera. Multivariable Cox regression models determined if these antibodies were independent predictors of outcomes (outcomes studied: acute rejection (AR) and graft failure (GF); other variables included in the model: DGF, AR (included only for GF outcome), ATG induction, donor type, HLA mismatch, recipient gender and age).
Results:

	No AT1R (n = 57)	AT1R (n = 19)	p
Recipient age, mean	45	44	0.837
Female recipient, %	39	63	0.062
Living donor, %	19	26	0.528
Previous KT, %	25	26	1
Previous pregnancy, %	16	42	0.026
HLA mismatch, mean	3.58	3.74	0.759
ATG induction, %	30	47	0.163
Delayed graft function, %	16	5	0.436
Anti-HLA antibodies, %	30	58	0.028
DSA, %	16	37	0.100
AR, %	12	37	0.017
Graft failure, %	7	37	0.004

Previous pregnancy was the sole significant (OR = 3.88, p = 0.022) risk factor for AT1R positivity in a multivariable logistic regression analysis.Graft outcomes according with DSA and/or AT1R presence status:

	No AT1R/No DSA (n=48)	AT1R/No DSA (n=12)	No AT1R/ DSA (n=9)	AT1R/ DSA (n=7)
AR, *n*	3	4	4	3
Cellular (Banff 1), *n*	3	–	1	–
Cellular vascular (Banff 2), *n*	–	3	–	–
Antibody-mediated, *n*	–	1	3	3

Conclusion: AR incidence was significantly increased in patients with AT1R, and even more in those with DSA. Presence of both DSA and AT1R was associated with the poorest graft survival rates, followed by AT1R-only. These data corroborate the possibility that a proper negative effect of AT1R on graft outcomes exists, besides a synergistic one with DSA, and both should be taken into account.



Clinical Kidney Rejection

BOS273 CLINICAL SIGNIFICANCE OF DE NOVO DONOR-SPECIFIC ANTI-HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION

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Background: The goal of this study was to investigate the impact of de novo donor-specific anti-HLA antibodies (DSA) on antibody-mediated rejection (AMR) and characterize DSA leading to AMR in kidney transplant recipients (KTRs).
Methods: We included 174 KTRs without pretransplant anti-HLA antibodies. All the enrolled KTRs were prospectively screened for the development of de novo DSA every 3 months before 1 year posttransplant and annually thereafter. DSA were determined by Luminex assays and expressed as mean fluorescence intensity (MFI). AMR was diagnosed by indication biopsy of allograft.
Results: Of 174 KTRs, 17 KTRs (9.8%) developed de novo DSA during a mean follow-up of 32.3 ± 13.5 months. The average time to first detection of de novo DSA was 28.2 months after kidney transplantation. All of de novo DSA were against class II antigens (11 DQ, 1 DR, and 5 both). The mean number of DSA was 1.8 ± 1.2, ranging from 1 to 5 and mean MFI of DSA was 7277.6 ± 5320.4. Acute AMR occurred only in KTRs with de novo DSA compared to KTRs without de novo DSA (17.6% vs. 0%, p = 0.001). In the KTRs with acute AMR, allograft biopsy was performed 108.3 ± 95.5 days after development of de novo DSA. Allograft survival was not different between two groups. There were no differences in the number of DSA and mean MFI of DSA between de novo DSA positive KTRs with AMR and de novo DSA positive KTRs without AMR.
Conclusions: Regular immunological monitoring is needed in KTRs to detect DSA because de novo DSA increased incidence of acute AMR. Close clinical monitoring and prompt interventions are mandatory in KTRs with de novo DSA, regardless of the number and strength of DSA, to reduce allograft damage induced by AMR.

BOS274 THE EXPRESSION OF ANGIOTENSIN II TYPE 1 RECEPTORS (AT1R) IN MICROCIRCULATION OF RENAL BIOPSY FOR CAUSE MIGHT BE SIGNIFICANT

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The humoral activity of non-HLA antibodies (Abs) especially characterized by anti-AT1R Abs seems to be substantial. We decided to characterize the importance of the AT1R expression and their connection with renal transplant failure.

The aim of our study was to assess the occurence of AT1R and its association with renal transplant loss in patients who had a biopsy due to worsening of renal function with characterization of staining in glomeruli and peritubular capillaries.
Methods: Immunohistochemical expression of AT1R was assessed in the 170 renal transplant biopsies. Microscopic evaluation of AT1R expression. AT1R expression was analyzed in five compartments in renal transplant biopsies: (i) glomeruli, (ii) renal blood vessels (small and intermediate arteries), (iii) peritubular capillaries, (iv) tubular epithelium and (v) interstitium based on three-step scale (0: lack of expression, 1: low immunoreactivity 2: high expression). The expression in microcirculation was positive in patients with g+ptc≥1.
Results: We analyzed 118 renal transplant recipients for the expression of AT1R. The renal allograft biopsy was performed between 6 days and 24 years after transplantation and the diagnosis was based on Banff criteria. 4 patients (pts) presented expression in microcirculation. 1 pt with **ptc+** (positive) staining developed acute antibody mediated rejection (aAMR) treated with IVIG, Ph, rituximab with success. A total of 3 pts with **g+** staining had aAMR in 1 cases and cAMR (chronic AMR) in 2 cases. All 3 pts lost the transplant during 24 months after biopsy instead of intensive treatment. 1 was treated with bortezomib. All 4 mentioned pts had additional staining in tubular epithelium (**t+**).

The occurrence of AT1R staining in microcirculation was associated with the diagnosis of antibody mediated rejection and high graft lost. The AT1R in renal transplant recipients with transplant insufficiency were expressed mainly in tubules but in microcirculation seems to be very important.

BOS275 DOUBLE FILTRATION PLASMAPHERESIS AND THERAPEUTIC PLASMA EXCHANGE: EFFICACY AND SAFETY IN THE TREATMENT OF RENAL GRAFT ANTIBODY MEDIATED REJECTION

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There are several methods of the rapid removal of antibodies from patient's plasma, among which are double filtration plasmapheresis (DFPP) and therapeutic plasma exchange (TPE).

Prospective randomized study in 58 recipients with renal graft antibody mediated rejection (C4d+) was conducted. 28 recipients received treatment with DFPP method, 32 – with TPE method. All patients underwent 3–4 sessions. The cumulative effect of complete course of procedures was investigated.

The decrease in concentrations of IgG and IgM was significantly greater when using DFPP. Thus, the preferential removal of IgM could be of the great value in acute rejection treatment. When conducting DFPP, the loss of albumin was significantly lower (p = 0.01).

When conducting DFPP, the plasma replacement was not required, while during TPE abundant plasma replacement "drop for drop" or more was necessary. As a result of abundant plasma replacement, the platelet count, INR (international normalized ratio), APTT (activated partial thromboplastin time), fibrinogen remained within the normal range. At the same time, DFPP statistically significantly reduced the levels of fibrinogen concentration (p = 0.01). Consequently, the patients with baseline deficiency of fibrinogen had the increase in bleeding risk.

Both TPE and DFPP contribute to the decrease in C0 of tacrolimus in blood of about 15-20%. In this regard, the correction of drug doses is required.

Rebound effect was observed when conducting DFPP, if less than 100% of volume of circulating plasma was processed during one procedure, and less than 70% of volume of circulating plasma were removed during conventional TPE. In this case, the effectiveness of even the whole course of treatment was low.

DFPP, as well as TPE are effective methods of the treatment of humoral rejection of renal graft only in case of sufficient dose of the procedure. Due to various influence on the biochemical parameters and hemostasis, indications for TPE and DFPP can vary considerably.

BOS276 GLOMERULOCAPILLARY MIRNA EXPRESSION PROFILES IN THREE DIFFERENT MODELS OF ANTIBODY-MEDIATED REJECTION (ABMR)

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Antibody-mediated rejection (ABMR) is still a diagnostic problem in kidney transplantation, its pathophysiology incompletely understood. miRNAs can be quantified from minimal amounts of paraffin- embedded biopsies and negatively regulate entire gene sets. We examined a rat model, an in vitro model of ABMR and human biopsies with thrombotic microangiopathy (TMA) due to ABMR for diagnostic glomerulocapillary miRNA expression signatures.

The Fischer F344 to Lewis rat model of renal transplantation and an in vitro model of anti-HLA class I-ABMR with glomerular endothelial cells and microdissected glomeruli from paraffin-embedded human biopsies with TMA due to ABMR were investigated with low density qRT-PCR arrays for differentially regulated miRNAs. Candidates were validated with single rRT-PCR runs in the rat model and TMA due to ABMR and on human biopsies with HLA class I-ABMR.

Two glomerular miRNAs were upregulated in the rat allografts (miR-199a-3p, miR-125b-2-3p), one was upregulated only in the isografts and remained at nontransplant control levels in allografts (miR-451-5p). In glomeruli of class I-ABMR 10 miRNAs were upregulated (let-7c-5p, miR-28-3p, miR-30d-5p, miR-99b-5p, miR-125a-5p, miR-195-5p, miR-374b-3p, miR-484, miR-501-3p, miR-520e) and 2 downregulated (miR29b-3p, miR-885-5p). A random forest analysis based on glomerular miRNA quantification allowed identification of 80–90% of patients with class I ABMR vs. controls. In TMA due to ABMR glomerular miR-532-3p was upregulated, its target ADAMTS13 downregulated on protein level. Glomerular miRNA quantification is a promising diagnostic technique for ABMR, complementing conventional histology. Interestingly, our three models exhibited a wide spectrum of deregulated glomerular miRNAs without any overlap that could be translated into novel therapeutic approaches.Clinical Kidney Immunology

BOS277 LONG-TERM PERSISTENCE OF ANTI-HLA ANTIBODIES IN RENAL TRANSPLANT RECIPIENTS: RISK FACTORS AND IMPACT ON CLINICAL COURSE

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Objectives: (i) To evaluate the incidence of development of anti-HLA antibodies (AHAB) on the long run in our renal transplant population and the main risk factors for their development. (ii) To investigate the impact of the antibodies on renal function and graft survival.
Method: A retrospective cohort study that included 372 patients that received a renal graft from 2005 to 2010. The analysis of AHAB was performed by Luminex®, with ≥2 determinations per patient.
Results: At a mean of 5 years post-transplantation, the presence of AHAB was detected in 30% (90/281) of our population: Class I 34.5%, Class II 29%, Class I and II 36.5%. Out of the pretransplant sensitized patients, 35/51 remained with positive antibodies after transplantation, while 55/230 no sensitized patients developed de novo AHAB. The risk factors for persistence/positive AHAB were: acute humoral rejection [4.23 (2.13–8.41), $p < 0.001$], pretransplant allosensitization [3.95 (2.37–6.55), $p < 0.001$], retransplantation [8.71 (4.26–17.79), $p < 0.001$], ≥4 HLA incompatibility [1.83 (1.02–3.42), $p = 0.049$], mean tacrolimus levels of <6 ng/ml [2.17 (1.12–4.92), $p = 0.048$]. There were no differences between different induction or maintenance immunosuppressants (30% with mTOR inhibitors). In the multivariate analysis, the independent factor for persistence of AHAB in pretransplant sensitized patients was having a previous transplant [13.50 (2.74–66.51), $p = 0.001$], while in those patients who developed de novo AHAB the main factor was having mean tacrolimus blood levels of <6 ng/ml [2.43 (1.09–6.72), $p = 0.047$). Patients who had Class I and II AHAB had worse renal function [eGFR 47 (19) vs. 54 (17) ml/min] and a lower 5-year graft survival rate (59.5% vs. 94.5%).
Conclusion: Allosensitization due to a previous transplant and low levels of tacrolimus seem to be the main risk factors for persistence or development of AHAB in the long-term. Their presence has a deleterious effect on clinical outcome, causing worse renal function and lower graft survival

Clinical Kidney Histology

BOS278 DETERMINANTS OF SEVERE FIBROSIS IN KIDNEY ALLOGRAFT: MAJOR IMPACT OF CIRCULATING DONOR SPECIFIC ANTI-HLA ANTIBODIES

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We investigated the independent contribution of circulating donor-specific anti-HLA antibodies (DSA) in the development of severe kidney allograft fibrosis with integration of traditional risk factors for allograft fibrosis.

We prospectively enrolled 1539 consecutive kidney recipients transplanted between 2004 and 2010, with systematic assessment of allograft fibrosis using the IF/TA Banff score on biopsies performed at 1-year post-transplantation. We considered all of the traditional determinants of allograft fibrosis reported in the literature, recorded at the time of transplantation and in the first year after transplantation. We also integrated DSA assessment and all the histologic diagnoses ("for cause" biopsies; $N = 1804$) performed in the first year after transplantation.

We identified 498 (32%) patients with severe IF/TA (Banff grade ≥2). DSA were associated with severe IF/TA at 1-year post transplant (adjusted OR, 1.53; 95% CI, 1.16–2.01; $P = 0.002$), independently of the traditional determinants, including: T cell-mediated rejection, antibody-mediated rejection, BK virus-associated nephropathy, calcineurin inhibitor toxicity, initial disease recurrence, pyelonephritis, acute tubular necrosis, donor and recipient baseline parameters, and transplant characteristics. DSA remained associated with severe IF/TA even in patients without episode of antibody-mediated rejection (OR, 1.47; 95% CI, 1.10–1.96; $P = 0.008$). Among the modifiable risk factors for severe IF/TA, DSA were found to be the first contributor, being involved in 11% of cases while T cell-mediated rejection, calcineurin inhibitor toxicity, acute tubular necrosis, pyelonephritis and BK virus-associated nephropathy were involved in 9%, 8%, 6%, 5%, and 4% of cases, respectively.

Circulating DSA are major contributor to severe allograft interstitial fibrosis independent of traditional risk factors and of antibody-mediated rejection.Clinical Kidney Rejection

BOS279 SECOND-LINE THERAPY AFTER STANDARD OF CARE IN ANTIBODY-MEDIATED REJECTION: A PROSPECTIVE STUDY

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There is a wide heterogeneity in antibody-mediated rejection (AMR) patients' prognosis after standard of care (SOC) including plasma exchange (PE) and intravenous immunoglobulin (IVIG). We investigated whether a composite prognostic score might identify patients at poor prognosis after AMR SOC therapy eligible for second-line intervention.

We prospectively included kidney recipients diagnosed with active AMR (2012–2014) who received standardized SOC therapy (PE x4 and IVIG 2 g/kg repeated every 3 weeks x 3). Patients were stratified according to their risk of graft loss after SOC based on an AMR prognostic score. High-risk patients received second-line treatment with complement-targeting agent (C5-inhibitor Eculizumab or C1-inhibitor Berinert) and high-dose IVIG for 6 months. The prognostic score was built in a prospective cohort of 284 kidney recipients with biopsy-proven active AMR receiving the standardized SOC therapy (abstract N° 3720943).

We enrolled 83 kidney recipients with active AMR diagnosed at a median time of 4.3 months post-transplantation. Patients received the SOC therapy, after which they were stratified in 3 risk groups defined according to the prognostic score. 15 (18%), 11 (13%) and 57 (69%) patients were stratified in the high-risk, intermediate-risk and low-risk groups, respectively. Predicted 3-year graft survivals after AMR were 94% (95% CI, 89–96), 64% (95% CI, 43–79) and 32% (95% CI, 17–48), respectively. The characteristics of high-risk patients were: GFR of 27.4 ± 8.9 ml/min, g+ptc Banff score of 4.1 ± 1.2 and DSA MFImax of 14482 ± 485 after SOC therapy, and 37.1 ± 10.5 ml/min, 3.5 ± 1.4 and 10319 ± 646 before SOC therapy. High-risk patients receiving second-line therapy showed a 3-year graft survival of 84%.

Risk stratification for kidney graft loss by a composite prognostic score based on clinical, histological and immunological parameters allows to identify high-risk patients after SOC treatment of AMR who may benefit from second-line strategies.

Clinical Liver Surgical technique

BOS280 NEW TECHNOLOGIES IN LIVER TRANSPLANTATIONS

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New Technologies in State Research Center Burnazyan Fmbc of The Fmba of Russia, Russian Federation

Aim: The immediate and long-term results of the liver transplantations at its terminal lesions have been studied.
Material and methods: 235 liver transplantations (LT) were performed in our Center between June 2010 and March 2017. 186 living donor liver transplantations (LDLT) have been performed. 49 cadaveric liver transplantations (CLT) have been performed (including adult split LT and retransplantations). 158 (67.2%) difficult LT have been performed. Complex reconstructions of the portal venous inflow or outflow have been required. Resections and reconstructions of the IVC and/or the right atrium by PTFE-conduits due to the parasitic lesions of the IVC have been performed. Isolated venous outflow from the 8 segment of the liver to middle hepatic vein, isolated venous outflow from the 6 segment of the liver and its diameters more than 5 mm were an indication for vascular reconstruction. Reconstruction and formation common embouchement of the portal vein via using autovenous Y-shaped portal conduit at "back table" was performed at trifurcation of the portal vein. Anastomosis between the portal vein of the recipient and autovenous portal conduit was formed for a short stump of the right portal vein of the transplant. Reconstruction of the portal vein at it complete fibrous obliteration was performed by autovenous prostheses. Saving the middle hepatic vein in the living donor's liver was a prerequisite.
Results: Mortality among recipients was 4.3%. Morbidity was 38.3%. Vascular complications after LDLT were 4.3%, after CLT were 0%. Frequency of the biliary complications (grade A, B (ISGLS, 2011) was 15.3% among all recipients. Mortality among living donors was not. The morbidity among living donors was 12.9% and was mainly represented of the bile leakage (grade A, B (ISGLS)). Postoperative hospital stay for recipients was 27 (23–32) days.
Conclusion: Presented technologies allow to achieve a good immediate and long term results of the liver transplantations.

BOS281 SPLENIC ARTERY STEAL SYNDROME IN PEDIATRIC LIVER TRANSPLANT: FIRST SERIES AND RESULTS

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Aim of the study: Splenic artery steal syndrome (SASS) is a known complication after adult liver transplantation (LT), with an incidence from 0.6% to 10.1%. To our knowledge, occurrence of SASS in pediatric LT has never been reported. Low hepatic artery (HA) flow in the absence of evident stenosis or thrombosis is associated to SASS. Blood preferentially flows from the celiac artery into the splenic artery (SA); the graft results relatively hypoperfused. The primary aim of this study is to evaluate the incidence of SASS in pediatric LT recipients and the efficacy of its therapeutic management. The secondary endpoint is to assess the association of SASS with vascular and biliary complications.
Methods: From December 2008 to April 2016, 146 consecutive children received a LT at Bambino Gesù Children's Hospital. Demographic, clinical and instrumental data of all recipients were retrospectively collected. All diagnoses of SASS were detected by Doppler-US and subsequently confirmed by angiography, if indicated.
Main results: Eleven patients (7.5%) were diagnosed with SASS; 4 intraoperatively and 7 post-operatively. SASS diagnosed on intraoperative Doppler-US were treated by SA ligation with immediate improvement of arterial flow in the graft. Postoperatively, diagnosis of SASS was suspected on Doppler-US data and confirmed by angiography. Percutaneous radiological approach allowed a prompt and effective treatment by proximal embolization of the SA in all cases. All children with SASS were successfully treated without consequences on graft function. Patient- and graft-survival rate is actually 100% after mean follow up of 43 months (range 7–76 months). No long term biliary and vascular complications were detected.
Conclusions: SASS seems underestimated in pediatric literature; however, in this series we report 7.5% incidence. Doppler-Us by experienced pediatric radiologists and a high degree of suspicion in selected cases play a key-role in early detection of SASS and avoi

BOS282 LIVER TRANSPLANTATION IN PATIENTS WITH PORTAL VEIN THROMBOSIS – IS IT SAFE?

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Background: PVT is a technical challenge for liver transplantation (LT) and thus often considered as contraindication. We evaluated the characteristics and outcome of patients with PVT and LT.
Methods: All patients with pre- or intraoperatively diagnosed PVT receiving a LT between 1994–2014 were included. Preoperative diagnosis, surgical therapy as well as patient- and graft survival were analysed.
Results: 53 patients (m:f = 40:13, mean age 52 ± 10) with pre- or intraoperatively diagnosed PVT were transplanted. Primary indications included alcoholic cirrhosis (38%), viral cirrhosis (23%), tumor (21%), biliary liver disease (9%) and others (9%). In 60% (n = 32) of patients, PVT was diagnosed preoperatively, and in 40% (n = 21) intraoperatively. Intraoperative observations revealed complete PVT in 16 patients (30%) and partial PVT in 37 patients (70%). Surgical therapy included thrombectomy in 83% (n = 44), an interponate in 7% (n = 4), another vessel for PV-anastomosis in 4% (n = 2) and fixation during the anastomosis in 6% of cases (n = 3). One- and 5-year patient- and graft survival was 82%, 76% and 75%, 69%, respectively. 8 patients (15%) experienced re-thrombosis after LT; this did not negatively impact patient- or graft survival. However, preoperative diagnosis of PVT (n = 32) and complete PVT (n = 16) significantly reduced graft survival in the early era after LT ($p = 0.047$ and $p = 0.018$, respectively). 16 patients (32%) solely received liver ultrasound during preoperative work-up, and in this group ultrasound failed to diagnose PVT in 75%. In contrast, in patients receiving liver US and CT or MRI, only 17.6% where not diagnosed with PVT (chi-square test<0.001).
Conclusion: In 60% of patients who received a LT, the diagnosis of PVT was established preoperatively. The majority of cases with PVT were successfully treated with intraoperative thrombectomy. However, the lower graft survival rates in cases with complete PVT, suggests a careful evaluation of this cohort prior to listing.

BOS283 SALVAGE LIVING DONOR LIVER TRANSPLANTATION FOR RECURRENT HEPATOCELLULAR CARCINOMA AFTER PRIOR LAPAROSCOPIC HEPATECTOMY: A PROPENSITY SCORE MATCHING STUDY IN A SINGLE INSTITUTE

Seok-Hwan Kim, Ki-Hun Kim, Shin Hwang, Chul-Soo Ahn, Gi-Won Song, Dong-Hwan Jung, Gil-Chun Park, Sung-Gyu Lee, Woo-Hyoung Kang Kang, Jae Hyun Kwon, Eunkyung Jwa, Hwui-Dong Cho, Su-Min Ha, Yong-Kyu Chung

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Background/Purpose: A salvage living donor liver transplantation (LDLT) for recurrent hepatocellular carcinoma (HCC) strategy that has been shown to be comparable to primary liver transplantation (LT). A previous hepatectomy may increase surgical difficulty by creating intra-abdominal adhesions. Laparoscopic hepatectomy (LH) reduce such technical consequences, but its effect on subsequent LDLT has not been reported. We study the operative results of salvage LDLT after laparoscopic and open hepatectomy (OH).
Methods: From January 2010 to December 2015, 112 salvage LDLT using right liver graft for recurrent HCC were performed, 9 following prior LH and 103 following prior OH. Indication for the salvage LDLT was recurrent HCC in all cases. In addition, to select a control group, propensity score matching (PSM) was used at 1:1 ratio with variables of patients characteristics.
Results: Mean durations of the time from skin incision to total hepatectomy were 426 ± 24.6 and 482 ± 58.2 mins in the LH and OH groups, respectively ($p < 0.05$). Median packed RBC transfusions during salvage LDLT were 0 (0–18) and 6 (0–32) U in the LH and OH groups, respectively ($p < 0.05$). These results were much same as that in PSM study. Mean post-operative length of stay was 19 ± 3.9 and 21 ± 14.7 days in the LH and OH groups, respectively ($p > 0.05$). In-hospital mortality was 2.9% (n = 1) only in OH group.
Conclusions: Salvage LDLT after LH for recurrent HCC is advantageous to OH in terms of operative time, blood loss and transfusion requirements. And our study also shows comparable outcomes in LH of oncologic results, morbidity and mortality to the OH group. We recommend the use of LH for primary HCC whenever it could be possible prior to LDLT.

BOS284 SHORT TERM OUTCOME IN LIVER TRANSPLANTATION AFTER DELAYED ABDOMINAL FASCIA CLOSURE

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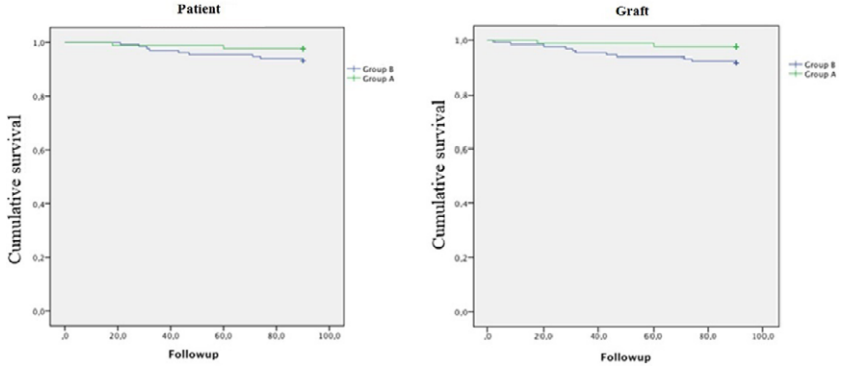
Background: Primary fascial closure is often difficult after adult liver transplantation (LT), complicated by donor-to-recipient graft size mismatch, coagulopathy and post-reperfusion hepatic or intestinal edema. The Miami



transplant Institute (MTI) has experienced a surgical approach consisting in a delayed abdominal fascia closure (DAC) in order to reduce the risks related to an increased intra-abdominal pressure.
Material/Methods: The aim of this retrospective study is to determine the influence of DAC on the 3 months outcome after LT. Were includes 219 adult LT performed at the MTI with MELD score ≥20 between January 2009 and December 2015. Patients were divided in a Group A (*n*: 87) subjected to DAC and a Group B (*n*: 132) as a control group. The mean of MELD score was 29.3 in group A and 27.9 in group B (p: 0.14). All data about donors and recipients' conditions, number of graft replaced arteries and back table artery reconstruction and also name of the surgeon were analyzed and were not recorded statistical significant differences. Three months follow-up was evaluated by blood tests and reporting any complications.
Results: During the follow-up 2 (2.3%) patients died in group A versus 9 in group B (6.8%). Thus, patients' survival was not significantly different in the two groups (p: 0.13) according to Kaplan Meier curve (Fig. 1). Instead, more cases of graft loss, without patient's death, were collected in group B than in group A [3 (2.3%) vs. 0 (0%)]. All these cases of graft loss were due to hepatic artery thrombosis (HAT) and this was significantly different (p: 0.048). HAT was the only one complication with a different incidence statistically significant (p: 0.006).
Conclusion: DAC leads to a reduction of intra-abdominal pressure, which seems to be associated with a reduction the incidence of graft loss and of major complications as HAT. Given our results a wider use of techniques that make it possible to reduce intra-abdominal pressure at the end of LT is desirable.

BOS285 CASE REPORT: FIRST DUAL GRAFT LIVER TRANSPLANTATION IN EGYPT

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Case-Presentation: Male patient 56 years old, father of 3 children, BMI = 35 presented with NASH-cirrhosis, moderate ascites, repeated spontaneous bacterial peritonitis (SBP) accompanied by hepatic encephalopathy, hepatorenal syndrome type-II, Child-Pugh (C11), and MELD = 23. He was listed for LDLTx, but multiple-donors were rejected due to small for size grafts.
Management and outcome: Major concern for small for size is high-BMI. After detailed family discussions to save their household's life, they had offered two-related donors instead of one. Dual-graft LTx on 22nd February, 2016, and the concept was to follow the natural instinct anatomy of the liver. Thus, donor-1 offered right graft volume = 550 cc (segment = 5,6,7,8), GRWR = 0.45, RLV = 45%; and donor-2 offered left graft volume 400 cc (segment = 2,3,4), GRWR = 0.4, RLV=60%. Both grafts were transplanted in respect to normal anatomy, biliary anastomoses were single right to right and single left to left ducts, similarly arterial and portal anastomoses. The right hepatic vein, V6-Makuuchi, and the left graft vein anastomosed directly to IVC while V5 with umbilical-vein graft. Portal vein de-clamping and grafts perfusion was performed after completion of vascular anastomoses of both grafts, to reduce injury induced by relatively high portal flow. The recipient stayed 7 days in ICU followed by 14 days in ward and discharged in good general condition and performance status for 1 year post-LTx. Also both donors were discharged safely after 10 days of post-operative hospitalization with smooth irrelevant clinical follow up.
Discussion: Although technically demanding, dual graft liver transplantation can offer safe solution for obese recipients avoiding small for size problem in absence of cadaveric program. Meanwhile, it provides sufficient RLV for donors' safety. Preoperative anatomical mapping and precise multidisciplinary team discussion are warranted to achieve best outcome.

BOS286 BALLOON ANGIOPLASTY IS EFFECTIVE IN THE MANAGEMENT OF STENOSIS OF HEPATIC VEIN OR INFERIOR VENA CAVA EARLY AFTER LIVING DONOR LIVER TRANSPLANTATION

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Hepatic venous outflow obstruction after living donor liver transplantation (LDLT) results from either intimal hyperplasia and fibrosis at the anastomotic sites or compression or twisting of the anastomosis due to graft regeneration. There is controversy regarding their management including balloon angioplasty versus stent insertion. During the period from April 2010 to February 2017, the authors experienced 3 (5%) cases of inadequate hepatic venous outflow among 58 cases of LDLT and report here. All the 3 patients were male who received modified right lobe graft and aged 53 to 58 years old. Their initial post-LDLT recovery was very smooth that 2 patients were discharged on postoperative day (POD) 13 and 14. Sudden onset of abdominal distension due to ascites was the first manifestation at POD 17, 15 and 20 in each. AST, albumin, bilirubin and creatinine level in each case was 95, 24 and 21 IU/l, 3.0, 3.0 and 2.0 g/dl, 0.5, 0.9 and 0.6 mg/dl and 0.9, 3.0 and 1.0 mg/dl, respectively. Hepatic venogram was performed under the suspicion of inadequacy in outflow.
Results: Hepatic venogram revealed some points of narrowing in the hepatic outflow pathway in these 3 patients and balloon angioplasty was performed. Results of balloon angioplasty were summarized in Table 1. There was no procedure-related complication. There was only small drop in pressure gradient with a single session of balloon angioplasty. All three patients, however, responded clinically as improvement in symptoms, diuresis and reduction in body weight and abdominal circumference 1–2 days after a single session of balloon angioplasty. Serum creatinine level was normalized in 1 patient who showed elevation before the procedure. No recurrence was found for 2 weeks to 11 months after the angioplasty. No patient required stent placement in this small series.
Conclusion: Balloon angioplasty was effective in the management of stenosis of hepatic vein or inferior vena cava early after LDLT.

BOS287 HIGHLY STRICT SELECTIONS OF DONOR REDUCE SURGICAL COMPLICATION AFTER LAPAROSCOPIC DONOR HEPATECTOMY

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Laparoscopic major hepatectomy is still innovative, and also laparoscopic donor hepatectomy is conducted in only several centers. In this study, we propose highly strict selection criteria for laparoscopic donor hepatectomy to reduce surgical complications.

From May, 2013 to Jan. 2017, we conducted 72 cases' consecutive laparoscopic living donor hepatectomy. After early trial and error, we had a strict indication on donor's selection- normal anatomy (type 1 bile duct, type 1. Portal vein). Nevertheless in some cases biliary complications were shown despite strict selection. And so we reviewed all donors' biliary anatomy and classified by length of neck of right bile duct (1 cm).

In this study, 64 donors enrolled in laparoscopic donation of right liver. And we classified by the length of right bile duct (from bifurcation of right/left bile duct to bifurcation of anterior/posterior bile duct) In group 1, 42 donors enrolled with the length of right bile duct is over 1 cm, and group 2 was consisted with 22 donors (short length of right bile duct <1 cm)

By statistical analysis, group 1 showed only 1 donor's biliary leakage from cystic duct (2%) but this complication was controlled by laparoscopic exploration. In contrast to long bile duct, group 2 was shown 6 donor's biliary leakage and 1 donor's biliary stricture. (32%) one complication was successfully controlled by laparoscopic suture of leaked bile duct, and other complicated donors were managed with endoscopic retrograde biliary drainage procedure without any long-term complication.

In laparoscopic donor hepatectomy, highly strict selection by donor's biliary anatomy - type 1 bile duct plus length of right bile duct over 1 cm - will help to reduce donor's biliary complications.

BOS288 RESULTS OF BILIARY RECONSTRUCTION WITH PTFE GRAFT IN LIVER TRANSPLANTATION

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Introduction: Biliary complications are often referred to as the 'Achilles heel' of liver transplantation (LT) with their high incidence rate, the need for repeated and long treatment, and the potential effects on graft and patient survival. The main problem is the development of fibrosis in the anastomotic area. By decreasing the rate of fibroses on both sides, it is possible to prevent biliary complications from developing. In our experimental study on pigs, we showed that by using spiral polytetrafluoroethylene (PTFE) graft, the complication rates dropped to almost zero. As such, we now use this technique as standard procedure in a clinical setting. To date, we have performed this technique with PTFE graft in 16 patients. In this study we aimed to review the results.
Materials and Methods: Between December 8, 1988 and March, 2017 we performed 565 LT procedures at our centers (age range, 6 months–64 years). Of these, 401 were living donor LT (71%), 167 were deceased donor LT (29%). We used PTFE graft in 16 patients. PTFE grafts were used in biliary stricture reconstruction after LT in 6 of these patients and in primary liver transplantation in the remaining 10 patients.
Results: Six patients are doing well with normal liver function after biliary stricture reconstruction. In the remaining 10 patients; 2 patients died due to sepsis with normal liver function. The remaining 8 patients are doing well with normal liver functions.

Conclusions: Biliary anastomosis using spiral PTFE graft is feasible with satisfactory anastomotic circumference and histologic evidence of healing. Our experimental studies as well as our small series of patients show that use of spiral PTFE graft is effective in reducing biliary complications in clinical transplantation.

BOS289 A CASE REPORT: HANGING HEPATOATRIAL ANASTOMOSIS IN CADAVERIC DONOR LIVER TRANSPLANTATION FOR A BUDD-CHIARI SYNDROME PATIENT

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The liver transplantations for Budd-Chiari syndrome (BCS) patients are challenging for variety of reasons. There is no standardized procedure for the reconstruction of the diseased hepatic vein or inferior vena cava (IVC) segments. The underlying hypercoagulable state or hematologic disorders in BCS patients may, also, raise problems during postoperative period. Although anastomotic failure of hepatic vein is an unusual complication in adult orthotopic liver transplantation (OLT), pre-existing inferior vena cava abnormality, such as in BCS, may contribute to the increased rate of the hepatic outflow complications. Technical adjustments are to be made in such cases.

We have experienced a deceased donor liver transplantation performed in BCS patient whose inferior vena cava was obstructed completely. For graft implantation, the upper cuff of the donor IVC was sutured directly to the right atrium and the lower cuff was closed by oversewing. No subsequent complication relevant to this vascular anastomosis was observed during six months of follow-up period. The pre-formed collateral vessels that diverted venous blood flow from the lower extremity and both kidneys to the superior vena cava through lumbar, azygos-hemiazygos system have played an important role in this successful transplantation.

BOS290 PORTAL VEIN ARTERIALIZATION AFTER TOTAL HEPATIC DE-ARTERIALIZATION IN LIVING DONOR LIVER TRANSPLANTATION: CASE REPORT

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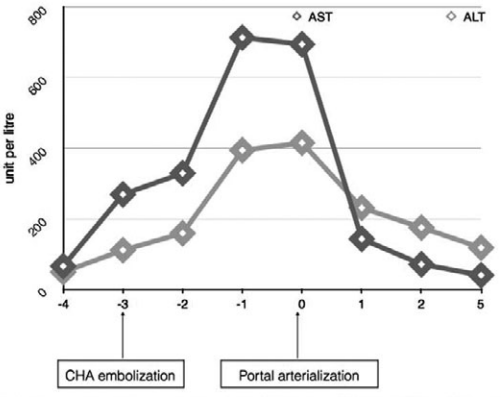
The recipient was 59 years old male with hepatitis B cirrhosis, single early HCC and portal vein thrombosis. He received extended right lobe graft from his son. In the operation, right hepatic artery was anastomosed to the hepatic artery proper and right portal vein to the main portal vein with intra-operative portal vein stent. Early post operative period liver function and clinical symptom was recovered rapidly. Post operative day 9th, he was diagnosed acute aortic dissection Stanford A with cardiac arrest. After 2 cycles of cardiopulmonary resuscitation, he returned of spontaneous circulation and received aortic arch replacement with circulatory arrest. Following the second operation, his clinical symptom and liver function was improved gradually then turned to normal. One month later, he experienced massive upper gastrointestinal hemorrhage with unstable vital signs. From esophagogastroduodeno-scope, we found massive bleeding from duodenum, after that, angiogram was performed. Finding was active bleeding from gastroduodenal artery to duodenum then coil embolization at common hepatic artery was performed. After embolization the bleeding was stopped, vital signs returned to normal but liver function got worse rapidly. We decided to re-operation to re-anastomosis the hepatic artery but cannot be achieved due to extensive thrombosis of the donor right hepatic artery. So, we performed portal vein arterialization by anastomosed common hepatic artery to splenic vein with end-to-side fashion. During the early postoperative period liver function was gradually improved. Unfortunately, there was no deceased donor during that period and finally, he died from uncontrolled intra-abdominal sepsis and liver abscess one month later. Portal vein arterialization may be a beneficial option for patient whom hepatic artery reconstruction is impossible.

Figure 1 shows AST and ALT related to total de-arterialization and portal arterialization



CHA = Common hepatic artery, AST = Aspartate aminotransferase, ALT = Alanine aminotransferase

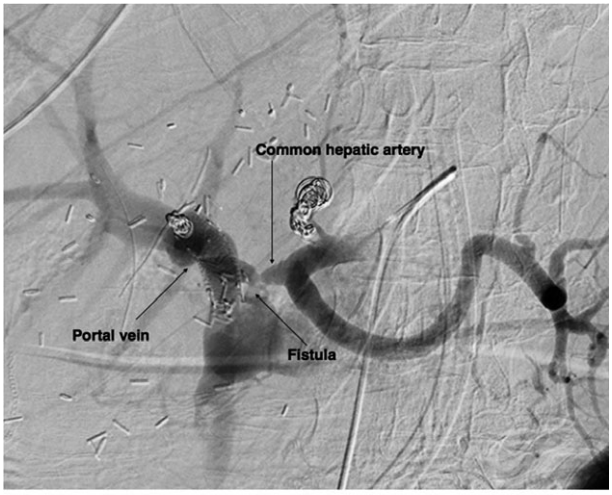


Figure 2. Angiogram from celiac axis demonstrates the created fistula

BOS291 IMPACT OF BILIARY DUCT RECONSTRUCTION TECHNIQUE ON LIVER TRANSPLANTATION OUTCOME

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Introduction: Biliary complication after liver transplantation remains high.
Aim of the study: To study the impact of the technique of biliary duct reconstruction on the outcome of liver transplantation.
Materials and methods: We retrospectively reviewed 65 patients who received full size liver graft from August 1, 2015 to December 1, 2016. Biliary reconstruction was performed by side-to-side (SS) and end-to-end (EE) anastomosis. Biliary complications, anastomotic stenosis, bile leak, acute rejection rate, and readmission within 90 days after surgery were evaluated by studying our patents records. In case of biliary complication, patients were selected, assigned to different complication-groups and subsequently reviewed in detail.
Results: A total of 65 patients (age: 57 (19–72)), were included in this study. The median follow-up was 7 months. 44 patients had end to end duct to duct biliary reconstruction, 21 had side to side anastomosis. Patients who had SS technique biliary anastomosis, MELD score was 28 while patient with duct to duct anastomosis MELD score was 24 ($p = 0.025$). The overall biliary complication rate was 9.4% ($n = 4$). 1 patient from each group had biliary leakage after (side to side anastomosis (4.8%) and end to end duct to duct (2.3%) biliary duct reconstruction. However, biliary leaks observed only in end to end anastomosis (2.3%) technique group which was not statistically different. Acute rejection episode observed in 3 patients (6.8%) with end to end biliary duct reconstruction, only 1 patient (4.8%) had AR with side to side biliary reconstruction group (p = ns). Readmission rate within 90 days after LT was similar 45.5% and 42.9% (p = ns) in end to end and side to side biliary duct reconstruction respectively.
Conclusion: Our study shows that biliary reconstruction technique seems to have little impact on the development of biliary complication in short time period. However, long term effect is needs to be studied.

BOS292 ANASTOMOSIS OF PORTAL VEIN AND BILE DUCT ANOMALY IN LIVING DONOR LIVER TRANSPLANTATION

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Chungnam National University Hospital, Republic of Korea

Introduction: We report our experiences of type 2 portal vein and bile duct anastomosis during living donor liver transplantation

Case: Forty-four years old man was admitted for generalized weakness. He suffered from CVH-B for 20 years and 2 years ago diagnosed LC with HCC. Primary HCC was treated by percutaneous RFA and recurred HCC was by TACE twice. After TACE generalized weakness, ascites were progressed. Hepatic encephalopathy was developed. Living donor liver transplantation was decided. Donor was 27-year-old son. GRWR was 1.48. Preoperative donor abdomen CT scan was revealed trifurcation of portal vein and low-lying right posterior hepatic duct. Middle hepatic vein branches were double in S5 and single in S8 level. Donor hepatectomy was performed as modified extended right hepatectomy (weight = 850gm). During bench operation neo-middle hepatic vein was reconstructed by use of iliac vein allograft. Lumens of graft portal vein were double. So left saphenous vein autograft patch was fenced to the graft portal veins for making single lumen. Graft was transplanted to recipient from right hepatic vein, portal vein, neo-middle hepatic vein and then right hepatic artery. Bile ducts were make common cannel in manner of V-shaped plasty then anastomosed to recipient bile duct. Total operation time was 632 minutes cold ischemic time was 40 minutes for bench operation. Maximal AST/ALT was 230/207 IU/ml at POD #1 then normalized at POD #5 and #15 each. Postoperative abdomen CT revealed patent portal vein, neo-middle hepatic vein and hepatic artery. There was no congestion area in the transplanted liver. Patient was discharged at POD #34. There was no stricture or stenosis in anastomosis site in veins, artery and bile duct.
Conclusion: In the living donor liver transplantation, there were many anatomical difficulties in anastomosis due to anatomical variation especially in portal vein and bile duct. Portal vein fencing and bile-ductoplasty can be a good choice.

BOS293 PIGGYBACK OR CAVA REPLACEMENT – WHICH TECHNIQUE IS PROTECTIVE AGAINST ACUTE KIDNEY INJURY AFTER TRANSPLANTATION? A SINGLE CENTRE ANALYSIS OF 431 CASES

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Background: The cava-preserving piggyback technique requires only partial cava clamping and therefore maintains venous outflow from both kidneys during the procedure. Compared to the classic cava replacing transplant technique, piggyback is considered to protect the kidneys from acute kidney injury (AKI) following transplantation. The aim of this study was therefore to compare kidney injury after liver transplantation with either piggyback or classic liver transplant technique.
Methods: We retrospectively analyzed pre-, intra- and postoperative data from patients ($n = 431$) undergoing liver transplantation from DBD donors between 2009–2016 at Royal Free Hospital, London. Among them 191 (44.3%) underwent piggyback technique and 236 (54.7%) cava replacement. General outcome and kidney function were assessed 5 days, 3 months and 12 months post-transplant. The overall follow-up was 4 years.
Results: Donor and recipient characteristics, e.g. donor age and cold ischemia time were comparable in both groups. The entire cohort was low MELD with a median of 16 points in both groups. ITU and hospital stay were comparable between both groups. Four-year graft and patient survival were similar comparing both groups. Importantly, despite longer cava clamping, kidney function following classical transplant technique was not inferior to piggyback at 5 days, 3 months and 1 year after transplantation. Transient renal replacement therapy (RRT) was required in 29% of cases following piggy back compared to 27% of cases after classic liver transplantation ($p = 0.819$).
Conclusion: Both surgical techniques are equal in terms of short- and long-term kidney function following transplantation.

Clinical Kidney Immunosuppressive agents

BOS294 COSMOS: A MULTICENTER, RANDOMIZED, OPEN-LABEL, PHASE IV STUDY OF KIDNEY TRANSPLANT PATIENTS CONVERTED FROM CICLOSPORIN TO PROLONGED-RELEASE TACROLIMUS PLUS STANDARD OR REDUCED-DOSE CORTICOSTEROIDS

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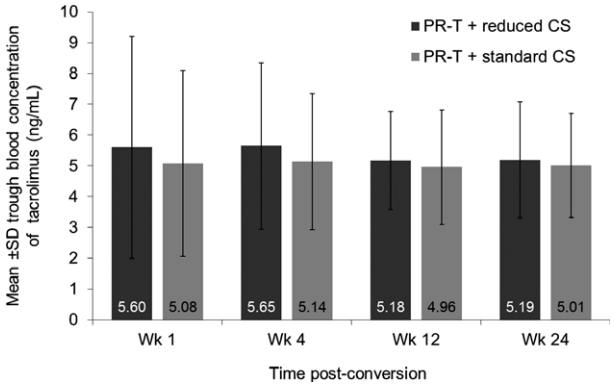
Background: Converting kidney transplant patients (KTP) from ciclosporin (CsA) to prolonged-release tacrolimus (PR-T) with concomitant corticosteroid (CS) dose reduction has not been studied.
Methods: Multicenter, comparative, open, Phase IV, 24-week (Wk) study (NCT02034747) conducted in stable adult KTP in Korea. At baseline (BL), patients were converted from CsA to PR-T 0.05–0.07 mg/kg/day and randomized (1:1) to maintain their CS dose, or undergo 50% dose reduction from Wk4 post-BL. Primary endpoint: change in estimated glomerular filtration rate (eGFR; Modified Diet in Renal Disease) from BL to Wk24, within/between arms. Secondary endpoints: creatinine clearance, acute rejection incidence, patient satisfaction with PR-T-based immunosuppression, laboratory tests, adverse events (AEs).
Results: 149 patients (mean ± standard deviation (SD) age 52.0 ± 10.2 years) converted to PR-T and received reduced ($N = 72$) or standard ($N = 77$) CS doses from Wk4. PR-T trough levels shown in Figure. Mean eGFR and creatinine clearance increased from BL to Wk24 in both arms, but achieved statistical significance only for eGFR with standard CS dose ($p = 0.0065$; Table). Differences between arms were not statistically different. No acute rejection episodes were reported. Overall, 70.4% of patients taking reduced CS doses were satisfied with PR-T convenience at Wk24 versus 82.4% taking standard doses; 45.5% of all patients reported missing fewer doses post-BL than pre-BL. While change from BL to Wk24 differed between arms for platelet count ($p = 0.0236$), high-density lipoprotein ($p < 0.0001$) and glycated hemoglobin ($p = 0.0173$), Wk24 levels were within normal range. Incidence of AEs, adverse drug reactions, severe AEs and withdrawal due to AEs were similar between arms.



Parameter	PR-T + reduced CS (*N* = 72)	PR-T + standard CS (*N* = 77)	p Value for difference between arms
Mean ± SD eGFR at BL, ml/min/1.73m^2	61.79 ± 17.54	62.47 ± 14.95	0.7997
Mean ± SD eGFR at Wk24, ml/min/1.73m^2	63.17±19.31	64.94±17.47	0.5988
Mean ± SD difference (BL to Wk24, or last observation carried forward) in eGFR, ml/min/1.73m^2	1.53±9.07	3.39±10.63	0.2538
P value for difference in eGFR (BL vs. Wk24) within arm	p=0.1567	p=0.0065	–

Conclusion: Renal function was maintained after conversion from CsA to PR-T-based immunosuppression, irrespective of CS dosing regimen. PR-T provides convenient once-daily dosing with potential for CS dose reduction.

BOS295 PROLONGED-RELEASE TACROLIMUS IN DE NOVO AND LONG-TERM KIDNEY TRANSPLANT PATIENTS IN ROUTINE CLINICAL PRACTICE IN AUSTRIA: THE STERN STUDY

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Background: To inform the medical community, real-world data supplement those from interventional studies. This study assessed the effectiveness and tolerability of prolonged-release tacrolimus (PR-T) in kidney transplant patients (KTPs) in routine clinical practice in Austria.
Methods: A prospective, non-interventional, 12-month, multicentre study at nine transplant centres in Austria. Adult KTPs, receiving PR-T *de novo* immediately post-transplant, or long term after conversion from immediate-release tacrolimus (IR-T), plus mycophenolate mofetil (MMF) and steroids, were included. Patients attended four routine clinic appointments: at baseline, and at 3, 6 and 12 months. Kidney function (estimated glomerular filtration rate (eGFR) by modification of diet in renal disease 2, serum creatinine), biopsy-confirmed acute rejection (BCAR), steroid dose, concomitant drugs and adverse events (AEs) were assessed.
Results: Of 157 KTPs recruited (63.7% male; mean age 51.8 years; 2.9 years (range 0–23.8) post-transplant), 6 received *de novo* PR-T and 151 had converted from IR-T. Mean daily PR-T dose (mg/kg) was similar throughout the study, while tacrolimus trough levels decreased from baseline to Month 12 (Figure). One conversion patient had BCAR at Month 3, and two had BCAR at Month 12 post-baseline. Mean eGFR (50.4–52.2 ml/min), creatinine (1.6–1.7 mg/dL), and the proportion of patients with proteinuria (13.4–17.8%) were similar across visits (Table). Most patients (75.2–82.8%) did not have infections requiring therapy. Median steroid and MMF doses were stable during the study (Month 12: 5 mg/day and 1 g/day, respectively). Eleven AEs were recorded in 10 patients, including five serious AEs. Five AEs were suspected of being treatment related.

Parameter	Baseline	Month 3	Month 6	Month 12
BCAR (*n* = 157), *n* (%)				
0	129 (82.2)	131 (83.4)	133 (84.7)	120 (76.4)
1	8 (5.1)	1 (0.6)	0 (0.0)	2 (1.3)
2	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	19 (12.1)	25 (15.9)	24 (15.3)	35 (22.3)
Proteinuria (*n* = 157), *n* (%)				
Yes	22 (14.0)	28 (17.8)	21 (13.4)	22 (14.0)
No	82 (52.2)	76 (48.4)	73 (46.5)	68 (43.3)
Missing	53 (33.7)	53 (33.7)	63 (40.1)	67 (42.7)
Creatinine (mg/dl)				
n	154	151	145	138
Mean (SD)	1.7 (0.9)	1.6 (0.7)	1.6 (0.7)	1.7 (0.8)
Median (minimum–maximum)	1.5 (0.6–7.0)	1.4 (0.6–5.3)	1.5 (0.7–4.9)	1.5 (0.7–5.4)
eGFR (ml/min)				
n	150	148	143	135
Mean (SD)	50.9 (21.8)	52.2 (20.2)	51.5 (19.8)	50.4 (20.6)
Median (minimum–maximum)	50.0 (10.0–120.4)	50.0 (13.2–117.2)	49.0 (14.3–118.7)	49.0 (11.2–100.0)

Conclusion: This real-world evidence on PR-T administration in Austria demonstrated stable renal function and few BCAR events; AEs were consistent with previous reports and PR-T was generally well tolerated.

BOS296 HIGH TACROLIMUS CLEARANCE IS A RISK FACTOR FOR ACUTE REJECTION EARLY AFTER RENAL TRANSPLANTATION

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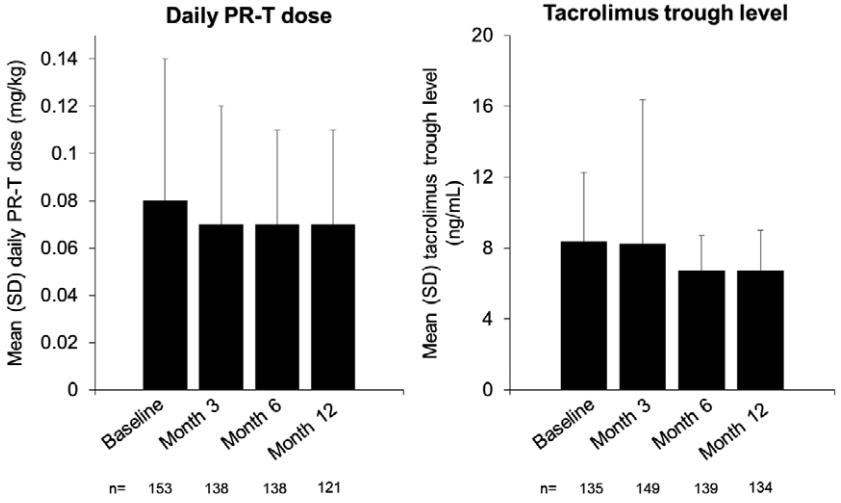
Background: Patients with high tacrolimus (Tac) clearance eliminate more drug within a specific dose interval. Missed and also delayed doses will result in transient periods of lower Tac concentrations in high- versus low clearance patients. Transient subtherapeutic Tac concentrations may induce acute rejection episodes.
Methods: A retrospective study in all renal transplant patients treated with Tac at our center from 2009 to 2013 was conducted. The association between individually estimated clearance (daily tacrolimus dose [mg]/trough concentration [μg/l]) and biopsy-proven acute rejection (BPAR) the first 90 days post-transplantation was investigated.
Results: In total, data from 638 patients treated with Tac were included in the analysis. During the first 90 days post transplantation 85 (13.3%) patients experienced BPAR, after a median (IQR) of 8 (5–31) days. Patients were stratified into four groups according to their estimated clearance. The patients



in the high clearance group showed significantly higher incidence of BPAR (20.6%) with a hazard ratio (HR) of 2.39 (95% CI; 1.30–4.40, $p < 0.006$) compared to the low clearance group (9.3%). Clearance estimate (as a continuous variable) had a HR of 2.25 (95% CI; 1.70–2.99, $p < 0.001$) after adjusting for other risk factors. There were no differences neither in trough concentrations the first week after transplantation nor in time to target trough concentration between patients experiencing BPAR or not.
Conclusions: High estimated Tac clearance is significantly associated with increased risk of BPAR the first 90 days post-transplantation and may be a useful clinical risk factor for prediction of rejection in the early phase following renal transplantation.

BOS297 IS ONCE-DAILY EXTENDED-RELEASE TACROLIMUS BETTER THAN TWICE-DAILY STANDARD-RELEASE TACROLIMUS? A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Tacrolimus is one of the major immunosuppressants commonly used in transplant recipients. Extended-release tacrolimus is expected to have immunosuppressant effects equivalent to standard-release tacrolimus while improving medication compliance. Here we conducted a meta-analysis on the comparison of outcomes of de novo transplant recipients using extended-release tacrolimus versus standard-release tacrolimus. There was no statistical significance between the two groups in the incidence of patient survival at both 6 months ($Z = 0.40$, $p = 0.79$) and 12 months ($Z = 0.45$, $p = 0.55$). No difference was found in the incidence of acute rejection and infection ($Z = 1.46$, $p = 0.14$ and $Z = 1.37$, $p = 0.17$). However, AUC24 h is much lower in once-daily extended-release tacrolimus group ($Z = 0.44$, $p < 0.05$), and the Cmax is much higher ($Z = 0.20$, $p < 0.05$). In summary, the current evidence suggests that once-daily extended-release tacrolimus has similar efficacy to twice-daily standard-release tacrolimus as an immunosuppressant but has lower AUC24 h and higher Cmax.

BOS298 COMPARISON OF ONCE-DAILY AND TWICE-DAILY TACROLIMUS FORMULATIONS IN DE NOVO KIDNEY TRANSPLANTATION – PHARMACOKINETIC AND ECONOMICAL ASPECTS

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The use of once daily tacrolimus formulations in *de novo* kidney transplant patients nowadays is common, even though this theoretically leads to later achievement of therapeutic blood levels and lower tacrolimus exposure. Therefore, we were interested in pharmacokinetic aspects of the use of novel once-daily tacrolimus tablets (LCPT, Envarsus) and once-daily tacrolimus extended-release formulation (ER-Tac, Advagraf capsules) compared with twice-daily immediate-release tacrolimus capsules (IR-Tac, Prograf). Furthermore, we looked at the costs of different tacrolimus formulations.

Recipients of a kidney allograft receiving a tacrolimus based immunosuppression were included in a single center retrospective study. For comparison daily doses (mg), doses per body weight (mg/kg), trough concentrations (ng/ml) and dose-adjusted trough concentrations (ng/ml/mg daily dose) were studied over 12 months. For the calculation of tacrolimus costs list prices and most convenient number of tablets/capsules were used.

We analyzed the data sets of $n = 21$ LCPT-patients, $n = 23$ IR-Tac-patients and $n = 36$ ER-Tac-patients. All pharmacokinetic comparisons between once-daily tacrolimus formulations revealed significant advantages for LCPT (Table 1).

The variability of trough levels (ng/ml) and dose-normalized trough levels (ng/ml/mg) in general is high and highest in LCPT-patients. The differences in pharmacokinetic characteristics translate into different treatment costs. These differences are highly significant during the early treatment phase. Given the daily treatment costs at 12 months the estimated costs per year add up to 6092 € for LCPT, 8594 € for IR-Tac and 7440 € for ER-Tac.

LCPT is superior over ER-Tac with respect to pharmacokinetic aspects and treatment costs.

	d10			d90			d360		
	Dose (mg)	Dose (mg/kg)	C/D ratio (ng/ml/mg)	Dose (mg)	Dose (mg/kg)	C/D ratio (ng/ml/mg)	Dose (mg)	Dose (mg/kg)	C/D ratio (ng/ml/mg)
LCPT	10.0 (6.75-14.0)	0.12 (0.08-0.18)	0.99 (0.66-1.84)	4.5 (3.0-5.0)	0.06 (0.04-0.07)	2.24 (1.63-3.24)	3.0 (2.25-3.50)	0.04 (0.03-0.06)	2.18 (1.59-3.47)
IR-Tac	15.0 (10.0-20.0)	0.19 (0.14-0.24)	0.59 (0.40-0.69)	6.0 (4.75-11.0)	0.09 (0.06-0.13)	1.40 (0.74-1.75)	4.5 (3.0-9.0)	0.05 (0.04-0.11)	1.60 (0.87-1.96)
ER-Tac	15.5 (13.0-18.75)	0.22 (0.18-0.26)	0.49 (0.38-0.69)	7.0 (4.0-8.5)	0.09 (0.06-0.14)	1.34 (0.96-1.94)	4.5 (2.75-6.75)	0.06 (0.04-0.11)	1.44 (0.92-2.35)
U-test (LCPT vs. IR-Tac)	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.05	P<0.05	P<0.05
U-test (LCPT vs. ER-Tac)	P<0.001	P<0.001	P<0.001	P<0.01	P<0.01	P<0.01	P<0.05	P<0.05	P<0.05
U-test (ER-Tac vs. IR-Tac)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Clinical Kidney Immunosuppressive agents

BOS299 IMMEDIATE INTRODUCTION OF EVEROLIMUS DOES NOT AFFECT WOUND HEALING AND DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS: 12-MONTHS RESULTS FROM NEVERWOUND STUDY

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Background: No robust data had previous evaluated the impact of immediate vs. delayed introduction of everolimus (EVR) on wound healing complications (WHC) in de novo kidney transplant recipients. The 3-months Core Analysis of the Study had shown that immediate introduction of EVR post-transplantation did not increase the risk of WHC. A long-term (FU-12M) wound healing complication incidence in the two groups has been here reported.
Methods: This open-label, multicenter study randomized 383 (1:1) single kidney transplant recipients to: immediate EVR (IE, 0.75 mg twice daily) along with low-dose cyclosporine (CsA, 4 mg/kg/day) or delayed EVR (DE, 0.75 mg twice daily) 28 ± 4 days after transplant along with low-dose CsA, with a bridge of enteric-coated mycophenolate sodium (1440 mg/day) and CsA (6–8 mg/kg/day). All patients received induction therapy and steroids as per local clinical practice. After a 3-month treatment period, patients were followed to re-evaluate the wound healing and efficacy.
Results: Proportion of patients without any WHC at 12 months was 67.9% and 69.5% in IE and DE groups respectively ($p = 0.75$). A statistically significant difference was found only for two subcategories of fluid collection, hematoma which was 7.8% vs. 2.6% ($p = 0.024$) and lymphocele which was 10.88% vs. 18.42% ($p = 0.037$) in IE and DE groups respectively. Treatment failure rate was 13% and 11% in IE and DE groups respectively ($p = 0.55$). No differences between the two groups were observed regarding patient and graft survival rates nor the occurrence rate and duration of DGF. The only hazard ratio that resulted to be statistically significant was BMI: HR was 0.66 (CI: 0.47; 0.92), meaning that BMI lower than 25 kg/m^2 decreased the risk of the first wound healing complication by 34%.
Conclusions: The immediate introduction of EVR post-transplant did not increase the risk of WHC. Renal function, efficacy, safety and tolerability were similar with both groups.

Clinical Liver Immunosuppressive agents

BOS300 EVEROLIMUS WITH REDUCED TACROLIMUS PREFERENTIALLY BENEFITS PATIENTS WITH IMPAIRED RENAL FUNCTION IN MAINTENANCE LIVER TRANSPLANT

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National Cheng Kung University Medical Center, Taiwan

Background: Chronic renal dysfunction is a frequent complication after liver transplantation. Results from prospective studies suggested that superior renal function can be observed with early introduction of everolimus (EVR), combined with reduced tacrolimus (Tac). Data from the maintenance liver transplant population is scarce.
Methods/Materials: A single center, retrospective study including 125 patients with primary liver transplants was conducted. Sixty-eight patients

were converted to the combination regimen of low dose EVR with Tac reduction at a mean of 7 months after transplantation (range 0.03–90 months). Forty-five recipients had eGFR (MDRD4) ≥60 ml/min (mean: 94) at time of EVR conversion, and 23 patients with the eGFR < 60 (mean: 45).
Results: Among 68 recipients with EVR conversion, the mean eGFR at time of conversion (M0), 12 months (M12) and 24 months (M24) after conversion was 80, 87 and 82 ml/min respectively. Recipients with better renal function (eGFR ≥ 60) had stable eGFR over 24-month follow up (eGFR at M0, M12, and M24 was 94, 100 and 98, respectively). In contrast, the significant change in eGFR was observed for patients with impaired renal function (M0 eGFR < 60). The mean eGFR increased after EVR conversion, with statistically significant difference from M1 through M18 (eGFR at M0, M1, M6, M12 and M18 was 45, 53, 55, 57 and 59 respectively, $p < 0.01$). Patients with EVR conversion within 6 months after transplantation had higher magnitude of eGFR improvement, compared to those with late EVR conversion. Monotherapy with EVR was only achieved in two patients, and no patient withdrawn from EVR treatment due to side effect. The incidence of biopsy proven rejection did not increase after EVR Demographics and characteristics of 125 liver transplant recipients conversion.
Conclusion: The study suggests that the combination regimen of low dose EVR with Tac reduction benefits patients with renal impairment in maintenance liver transplant. This protocol also provides acceptable safety profile and efficacy.

Clinical Kidney Immunosuppressive agents

BOS301 CLINICAL ANALYSIS OF CALCINEURIN INHIBITOR-BASED IMMUNOSUPPRESSIVE THERAPY COMBINED WITH EVEROLIMUS IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS

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In ABO-incompatible (ABO-i) kidney transplant patients, it is important to achieve long-term graft survival, as in ABO-compatible (ABO-c) kidney transplantation. Everolimus (EVR), a mammalian target of the rapamycin (mTOR) inhibitor, is suggested to preserve renal graft function. We assessed the efficacy of adding EVR to calcineurin inhibitor (CNI)-based immunosuppressive therapy in ABO-i kidney transplant recipients by comparing with ABO-c kidney transplant recipients. Twenty-seven ABO-i kidney transplant recipients who underwent surgery at Osaka General Medical Center, Japan, had EVR added to the CNI-based immunosuppressive regimen between October 2012 and July 2016, they were compared with 45 ABO-c kidney transplant patients who had also received EVR in the CNI-based immunosuppressive therapy. The median patient age in the ABO-c group and ABO-i group was 41 years (15–70 years) and 49 years (33–69 years), respectively ($p = 0.02$). There was no significant difference in other patient characteristics observed between the two groups. The estimated glomerular filtration rate (eGFR) measured at 3 months, 1 year, 2 years, and 3 years post-transplant in the ABO-i group were higher (45.6, 47.2, 46.6, and 46.3 ml/min/1.73 m^2, respectively) than in the ABO-c group (47.5, 45.6, 44.4 and 42.4 ml/min/1.73 m^2, respectively). Proteinuria was increased in both groups in comparison to before staring EVR. However, there was no significant difference in the eGFR and proteinuria over time in the two groups. There were two cases of clinical rejection, one in each group; EVR was discontinued in both cases. Additionally, EVR was discontinued in three ABO-c patients owing to renal dysfunction, even though they were not diagnosed with clinical rejection. The effect on renal function and the safety of immunosuppressive therapy with EVR in ABO-i kidney transplant recipients was similar to that observed in ABO-c kidney transplant recipients.

BOS302 THE USE OF SIROLIMUS IN PATIENTS WITH RECURRENT CYTOMEGALOVIRUS (CMV) INFECTION AFTER KIDNEY TRANSPLANTATION. A RETROSPECTIVE CASE SERIES ANALYSIS

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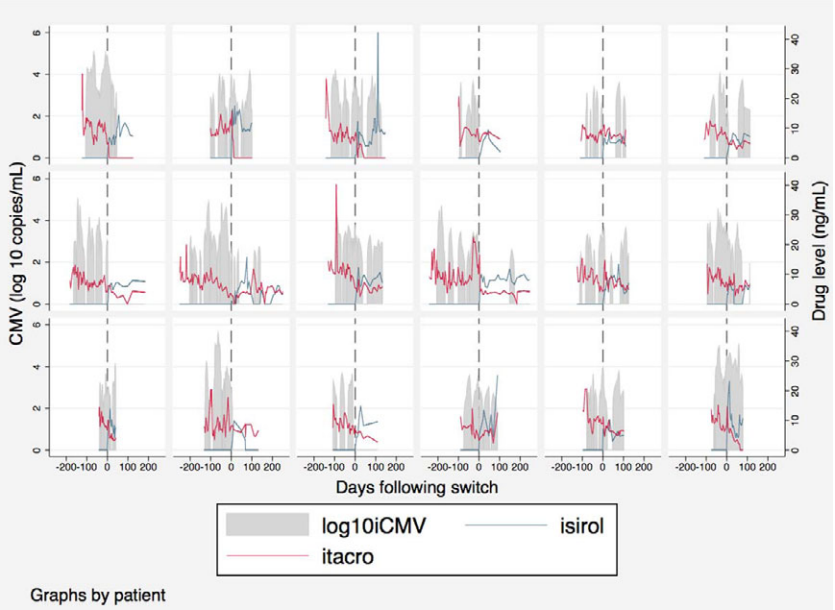
Background: CMV is the commonest opportunistic infection post-solid organ transplant and remains a cause of morbidity and mortality. Mammalian target of rapamycin (mTOR) inhibitors have a theoretical antiviral advantage compared to conventional immunosuppression (IS). We retrospectively analysed the outcome of substituting Sirolimus for MMF or tacrolimus in 18 kidney transplant recipients (KTRs) with difficult to manage, recurrent CMV viraemia (CMVv) unresponsive or intolerant of standard anti-CMV treatment (CMVT) or IS reduction.
Methods: We studied a cohort of 18 consecutive adult KTRs who were transplanted from 2009 to 2015 at the Royal Free London Hospital with recurrent CMVv who received pre-emptive therapy. KTRs with recurrent (>3) or prolonged episodes of CMVv, before the sirolimus switch, despite appropriate CMVT and implementing strategies to combat clinically suspected CMV resistance were included.
Results: 13 were males and 5 females with a median age at transplantation of 53 years (range 20–73). 14 patients (77.8%) had primary CMVv and the remaining 4 patients (22.2%) had either CMV reactivation or reinfection. The AUC for Log10 CMV viral load (log10 copies/ml) was significantly higher before than after the sirolimus switch ($z = 2.417$, $p = 0.0156$) (Image 1). Acute rejection occurred more commonly before starting sirolimus in the context of IS reduction (5 KTRs, 27.7%) while only 2 KTRs had rejection after conversion (11.1%). The median number of days on CMVT was reduced after conversion to sirolimus (48 days, range 0–95) as compared to before conversion (68 days, range 21–146). Median serum creatinine before conversion to sirolimus was 175.5 μmol/l (range 79–243), and showed no deterioration at 3 months after conversion at 148 μmol/l (range 69–271, p value: 0.002) and 162.5 μmol/l



(range 69–287, p-value: 0.002) at 1 year.**Conclusion:** In our experience, the use of a mTORi is a useful strategy in treating recurrent CMV viraemia without provoking rejection.

BOS303 COMPARISON OF MTORIS AND CALCINEURIN INHIBITORS IN LOW-IMMUNOLOGICAL RISK RENAL TRANSPLANT RECIPIENTS

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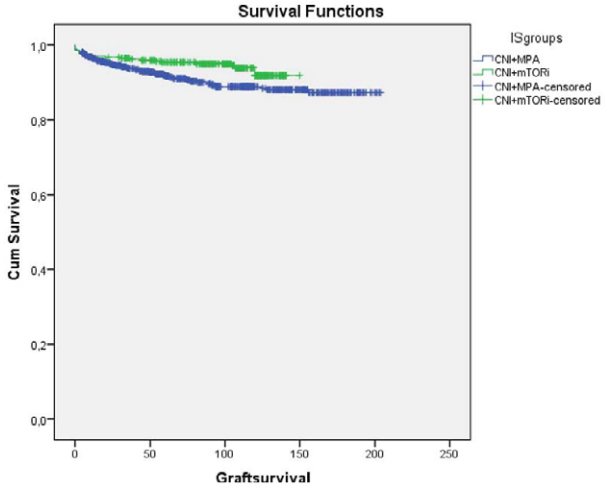
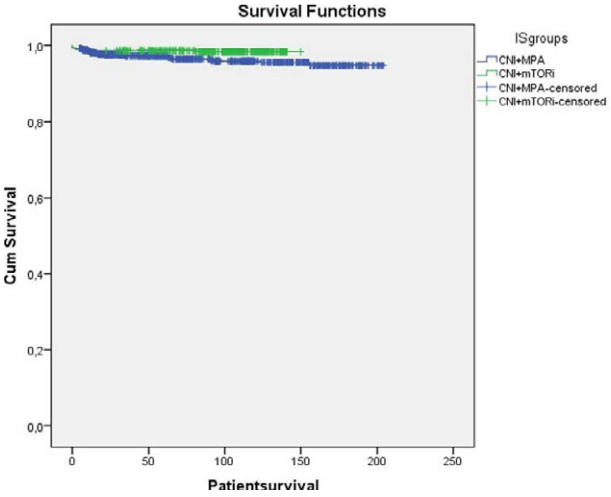
Background: This study was to evaluate the safety and efficacy of mTORis and calcineurin inhibitors (CNI) in low-immunological risk (mismatch numbers ≤3, 1 transplant, living donor) renal transplant recipients.
Materials and Methods: We included 1228 renal transplant recipients to study and divided two groups; Group 1: Full dose CNI plus mycophenolic acid (MPA) (*N*: 846, tacrolimus (TAC) based: 619, cyclosporine (CSA): 227, male/female: 559/287, mean age±sd: 33.5 ± 11.8), Group 2: mTORis plus low dose MPA after low dose CNI plus mTORis in the first three months (*N*: 382, 281/101, 34.1 ± 12.1, TAC+Sirolimus (SRL): 74, TAC+Everolimus (EVE): 53, CSA+EVE: 116, CSA+SRL: 139). There was no significant difference between the groups in terms of lymphocyte cross match and mismatch numbers. SPSS 20.0 software program was used for statistical analysis.
Results: Demographic features were similar between the groups. Graft survival rates (Figure 1, p: 0.016) and patients survival rates (p: 0.047) were significantly higher in group 2. Acute rejection rate (16%/20.2%, p: 0.06), posttransplant diabetes mellitus (p: 0.686), BK virus viremia and nephropathy (p: 0.939), cytomegalovirus viremia (p: 0.247) and chronic allograft dysfunctions (p: 0.388) rates were similar between the groups. Hemodialysis and plasmapheresis need after transplantation were higher in the group 1. In the last control, serum creatinine levels was similar (p: 0.077) between the groups. The amount of proteinuria (p: 0.001), serum albumin (p: 0.008), triglyceride (p: 0.043) and low-density lipoprotein (p: 0.001) levels were higher in the group 2.





Conclusion: This study showed that mTORis based therapy modalities in low-immunologic risk renal transplant recipients were more effective and safety according to CNI based therapies in terms of especially graft and patients survival.

BOS304 ALEMTUZUMAB (CAMPATHÂ®) VS. BASILIXIMAB (SIMULECTÂ®) AS AN INDUCTION THERAPY FOR RENAL ALLOGRAFT TRANSPLANTATION: 5-YEAR OUTCOME OF A SINGLE CENTRE

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Introduction: We compared alemtuzumab to basiliximab as an induction therapy. The Objectives of this study were to measure the renal graft survival, acute rejection rate, cytomegalovirus (CMV) infection, post-transplant lymphoproliferative disease (PTLD), diabetes mellitus (PTDM) and skin cancer in the two groups.
Method: A retrospective study of 101 patients over a period of 12 months from April 2011. The cohort was divided in two groups based on their immunosuppression induction therapy as alemtuzumab ($n = 50$), and basiliximab ($n = 50$). Patients excluded ($n = 1$) as lost to followup. Our standard immunosuppression induction therapy protocol was to use alemtuzumab in sensitised patients and basiliximab in negative crossmatch recipients. The maintenance immunosuppression were tacrolimus and mycophenolate without steroid.
Results: The overall graft survival among the cohort was 92%. Total graft loss was 8% of which 6% in the alemtuzumab group versus 2% in the basiliximab group. The causes of graft loss were graft thrombosis 2%, polyomavirus nephropathy 2%, acute graft rejection 1%, chronic graft rejection 1%, recurrence of membranous glomerulonephritis 1%, and hypercalcaemia 1%. The rate of biopsy-confirmed acute rejection was lower in the alemtuzumab 8% versus 18% in the basiliximab group. The graft loss secondary to acute rejection was 0% versus 2%, chronic rejection was seen in 2% versus 0% in the two groups, respectively. CMV viremia was higher in the Campath 46% versus 24% in the Simulect group, and PTLD was 6% versus 0% in the two groups respectively. The rate of post-transplant diabetes mellitus was higher in the alemtuzumab group 10% versus 2%. Skin cancer occurred in the alemtuzumab group only in 4% post-kidney transplant.
Conclusion: The 5-year follow-up results showed that, there were no significant difference between both groups in graft survival, and graft loss due to rejection was seen in 2% of each group. Overall, the Campath group had higher rate of PTLD, PTDM, CMV and post transplant skin cancer.

BOS305 AN ANALYSIS OF EFFECTS OF RITUXIMAB ON LIVING KIDNEY TRANSPLANTATION RECIPIENTS

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Background: For highly sensitized recipients such as ABO-incompatible recipients, rituximab is added to induction immunosuppressive therapy. However, rituximab increases the risks of infections or neutropenia. We aimed to examine whether rituximab could be used safely by comparing between patients who received and those who did not receive rituximab.
Methods: From 2009 April to 2015 November, 125 patients received living kidney transplantation in Ohkubo Hospital. Rituximab was administered to ABO-incompatible transplantation patients, recipients with donor-specific antibody, and patients with a history of blood transfusion or pregnancy. We compared the cases in terms of graft rejection, graft loss, death, infection, and neutropenia. Infections included cytomegalovirus (CMV), BK virus, varicella-zoster virus (VZV), adenovirus (AdV), and general bacterial infections.
Results: Seventy-nine patients received rituximab as an induction immunosuppressant, and 46 patients who did not. Neutropenia occurred in higher rates in the patients with rituximab (44% vs. 23%, p = 0.019). However, no significant differences in antibody-mediated rejection (9% vs. 2%), T-cell mediated rejection (15% vs. 15%), graft loss (2.7% vs. 2.1%), death (2.1% vs. 0%) and infections were found. Infection results showed CMV viremia (24% vs. 17%), VZV infection (11% vs. 8.6%), BK virus (7.5% vs. 0%), AdV cystitis (5.0% vs. 2.1%), and bacterial infection (31% vs. 34%), none of which showed significant differences.
Conclusion: Rituximab therapy increased the risk of neutropenia. However, the incidences of rejection, graft loss, death, and infection showed no

significant differences between those who received and those who did not receive rituximab. This suggests that it could be used safely as an induction therapy.

Clinical Others Immunosuppressive agents

BOS306 GENERIC SUBSTITUTION OF MYCOPHENOLATE MOFETIL-BASED IMMUNOSUPPRESSANTS

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Background: Mycophenolate mofetil (MMF), the ester prodrug of mycophenolic acid (MPA), is an integral part of an immunosuppressive therapy for the prophylaxis of acute organ rejection in recipients of allogeneic renal, hepatic, or cardiac transplants. Since its introduction in 1996 rejection rates have significantly reduced. With the advent of generic substitution of the originator product (CellCept®, F. Hoffmann-La Roche Ltd.) questions around biopharmaceutical and therapeutic equivalence occur.
Methods/Materials: A clinical study (NCT02981290) was performed in 32 healthy volunteers with the objective to compare in a four-period crossover design the pharmacokinetics of MPA following administration of CellCept® and three commercially available generic substitutions, Renodapt (Biocon Ltd.; referred to as compound A), Mycept (Panacea biotec; B), and Cellmune (Cipla Ltd.; C).
Results: The comparison of the generics between each other revealed substantial apparent differences in maximum concentration (C_{max}) of generated MPA; the geometric mean ratios for two of the generics each compared with the third were 15% (A vs. C) and 23% (B vs. C) below unity and the 90% confidence intervals were not included in the equivalence region of 80–125% around the reference mean. This raises doubts whether the generics would meet standard regulatory bioequivalence criteria when compared against each other in a formal bioequivalence study. The differences in Cmax paralleled the slower *in vitro* dissolution rates of A and B compared to C and to CellCept®.
Conclusion: Prescribing physicians in the field of transplantation should be aware of the potential risk of altering the therapeutic outcome when switching from one generic to another generic preparation of MMF.

Clinical Kidney Immunosuppressive agents

BOS307 IMPROVING UNDERSTANDING OF HEATH BELIEFS AND IMMUNOSUPPRESSION ADHERENCE IN LONG-TERM KIDNEY TRANSPLANT PATIENTS THROUGH PHARMACIST-LED CONSULTATION AND MEDICINES OPTIMISATION

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Introduction: Health beliefs in long-term (>7 years) kidney transplant patients (LKT) have been associated with immunosuppression (IS) non-adherence resulting in poorer transplant outcomes. The purpose of this study was to (i) identify the extent of IS non-adherence in a cohort of LKT; (ii) investigate the influence of health beliefs on IS adherence; and (iii) explore the potential of pharmacist-led consultation and medicines optimisation (MO) in this setting.
Methods: All LKT attending Transplant Clinic between 01/09/16 and 01/03/17 completed screening questionnaires, including adapted versions of (i) Medicines Adherence Report Scale (MARS) and (ii) Beliefs About Medicines Questionnaire (BMQ). All LKT were offered either face-to-face or telephone consultation with a renal pharmacist.
Results: 138 LKT were screened. Their mean age was 53.6 years (range 22–80 years). 55 (40%) were female. 129 (93%) screened were taking at least 2 IS medications.

130 (94%) patients agreed their health depended on IS. However 36 (26%) patients worried about taking IS and 41 (30%) reported unpleasant side-effects. 79 (57%) patients admitted forgetting IS, 6 (4%) avoiding IS, and 9 (7%) deciding to omit IS.

There were $n = 95$ pharmacist consultations (63 face-to-face, 32 telephone) resulting in MO in 58 (61%) patients. 29 (31%) patients were given repeat or amended IS prescriptions. 21 (22%) patients had in-depth IS adherence discussion. Of these 10 had prescription or timing of administration changes. 26 (27%) patients were offered other medicines advice, including vaccination and dosette box provision.
Discussion: Understanding about the importance of IS in this LKT cohort was good. However, a significant proportion is non-adherent. Our findings demonstrate considerable scope for a pharmacist-led MO consultation and intervention service focussing on adherence. Analysis to identify associations between health beliefs, IS adherence and MO is underway and will inform service implementation.

Clinical Kidney Surgical technique

BOS308 LAPAROSCOPIC PYELOURETEROSTOMY WITH RECIPIENTS URETER IN A TRANSPLANTED KIDNEY FOR URETERAL STRICTURE

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Introduction: Ureteral obstruction secondary to ischemia is the most common urologic complication of kidney transplantation. Pyeloureteral anastomosis with recipient ureter has shown most satisfactory long-term results in its management. Existing urinary infection and immunosuppression determine the high risk of wound complications. Till last time this procedure has been performed through open surgery, however in 2006 Orvieto M.A. et al. first reported minimally invasive approach using the Da Vinci robotic system.
Method: We have experience more than 30 procedures of ureteral strictures repair after kidney transplantation by open surgery during 20 years. Since February 2012 we used pyeloureteral anastomosis with recipient ureter in two patients by laparoscopic approach. The operations lasted 215 and 275 minutes respectively.

In both cases the surgery was performed after percutaneous nephrostomy because of deterioration of transplanted kidney function. Internal stent was indwelled laparoscopically. No drain tube was left.
Results: The nephrostomy tubes were removed after 7 and 10 days respectively. The stents were removed after 20 and 27 days respectively. No complications were seen during the surgery and postoperative period. Now serum creatinine level is 0.12 and 0.15 mmol/l after 15 and 12 months after surgery respectively.
Conclusion: In spite of some difficulties related with topographic landmarks and severe tissues fibrosis after transplantation laparoscopic pyeloureterostomy in transplanted kidney is safe and feasible procedure. The main advantage is absence of risk of most serious complications related with wound infection in immune compromised patients

Clinical Pediatric Transplantation Donation and donor types

BOS309 LAPAROSCOPIC APPROACH FOR LIVING DONOR TO PAEDIATRIC LIVER TRANSPLANT

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Objectives: Exposure of technical steps of the first case reported in Spain of purely laparoscopic left lateral sectionectomy for adult-to-paediatric living liver donation.
Patients and methods: The case of a living related donation from aunt to niece is exposed. The recipient had a cholestatic chronic liver insufficiency due to extrahepatic biliary atresia after a failed Kasai procedure.
Results: A purely laparoscopic approach of the left lateral section of the donor, which had a total volume of 281 cm^3 with 3.5 GRWR was performed. Total operating time was 5 hours with no need to perform any Pringle maneuver. Left hanging was carried out to facilitate the transection. The warm ischemia time was 9 minutes. Implantation was performed with caval preservation (piggy-back technique). The donor was discharged on the 4th day and the recipient was favorably discharged on the 16th post-operative day.
Conclusions: In highly specialized units, complex procedures such as major laparoscopic hepatectomies and minimally invasive approach to living donor can be safely performed. In our center, the last 5 adult-to-paediatric living donors have been performed laparoscopically, turning into our standard of practice, as recently reported.

Clinical Kidney Other

BOS310 A MYSTERIOUS PRESENTATION FOR SYSTEMIC LUPUS ERYTHEMATOUS EIGHT YEARS AFTER KIDNEY TRANSPLANTATION

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Case presentation: We are presenting a 45 years old female patient, who is 8 years' status post living unrelated donor kidney transplant. She was following in another hospital and referred for resistant hypertension and normocytic normochromic anemia. Her primary disease unknown, no information regarding her donor. According to the referral, her creatinine ranged between 160–180 mmol/l and stable around that value for the last years. BP was controlled by 3 antihypertensive medications but she develops massive lower limb edema, for that amlodipine changed with hydralazine. During that period the patients develop thrombocytopenia, investigation failed to show any viral infection. So mycophenolate mofetil was stopped. The patient developed a bilateral occipital headache, not responding to usual analgesic, Magnetic resonance imaging (MRI) showed hyperintense signals in the white matters. The patient was discharged after some improvement of her symptoms. One week later, she presented with a full-blown picture of SLE, with a typical malar rash skin lesion, nephrotic syndrome, pancytopenia, and all serological markers came positive. Kidney biopsy done showed combined class 4 and 5 lupus nephritis. MMF reintroduced again, and hydralazine was stopped with a disappearance of skin rash and marked decrease in proteinuria.
Discussion: The patient presentation is mysteries. Many questions need an answer. Is the initial presentation with resistant hypertension and anemia is a part of SLE or not? Did the addition of hydralazine just unmask SLE, or lead to drug-induced lupus? Which event was the actual trigger for SLE, the addition of hydralazine or the discontinuation of MMF?

So, is this recurrent of undiagnosed primary disease, de novo SLE, or drug-induced lupus?

Clinical Kidney Surgical technique

BOS311 KIDNEY TRANSPLANTATION FOLLOWING EX-VIVO RECONSTRUCTION OF THE RENAL ARTERY ANEURYSM WITH AN ARTERIAL PATCH

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Background: Increasing number of patients with end stage renal disease has led to an expansion of donor selection criteria. The use of kidneys from living donors with renal artery aneurysms (RAA) not only increases the number of organs available for transplantation but also is a treatment option for selected patients having RAA. This video presents a technique of RAA reconstruction with an arterial patch.
Materials & Methods: A 64 year-old male donor with a 1.5 cm saccular RAA at the branch of the left main renal artery has undergone a standard 4-port laparoscopic donor nephrectomy. The kidney was transferred to the bench side and perfused with UW solution. Renal artery irrigation distended the aneurysm clearly demonstrating at the bifurcation. The aneurysm was excised carefully. The posterior wall of the defect was repaired with running 6–0 polypropylene sutures. In order to prevent stenosis, "patch" of the anterior wall was decided. Appropriate length arterial segment was excised from the proximal healthy renal artery and used as a patch to reconstruct the anterior surface of the bifurcation with running 6–0 polypropylene sutures. Control irrigation revealed normal renal perfusion with no anastomotic leak or a saccular distention.
Results : The kidney was placed on the iliac fossa of the 28-year-old son. Following the anastomosis of the reconstructed artery in an end-to-end manner to the recipient's internal iliac artery, no anastomotic leak was observed and the kidney was evenly perfused.
Conclusion : Reconstruction of the renal artery aneurysms with various techniques including primary or venous patch repairs preceded with transplantation is an established issue in the transplantation literature. However, use of an arterial segment easily obtained from the proximal renal artery may offer stronger and and durable repair by preventing stenosis risk which may ensue with primary repair as well as complications of venous patches including increased stenosis and aneurysm formation in long term follow up.

BOS312 KIDNEY AUTOTRANSPLANTATION FOR COMPLEX RENAL ARTERY ANEURYSM REPAIR

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Insubria University, Italy

Intraoperative fluorescent imaging using indocyanine green enables vascular surgeons to confirm the location and states of the reconstructed vessels during surgery. Complex renal artery aneurysm repair involving second order branch vessels has been performed with different techniques. We present a case of ex vivo repair and autotransplantation combining the advantages of minimally invasive surgery and indocyanine green enhanced fluorescence imaging to facilitate vascular anatomy recognition and visualization of organ reperfusion.

BOS313 IMMEDIATE GRAFT NEPHRECTOMY AND RE-TRANSPLANTATION OF KIDNEY ALLOGRAFT FOLLOWING ACUTE RENAL VEIN THROMBOSIS

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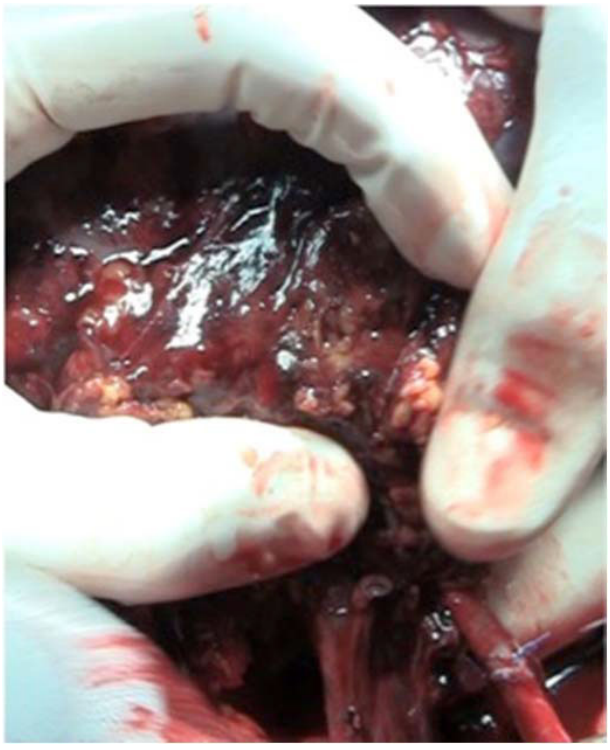
Background: Renal vein thrombosis (RVT) is usually associated with a technical problem. The dramatic presentation with oliguria, hematuria, and extreme patient discomfort may accompany life-threatening bleeding. In this video we present a case of immediate graft nephrectomy and re-transplantation of a recipient developing acute RVT following two hours after kidney transplantation (KTx).
Materials & Methods: An 18-year-old male recipient with a primary diagnosis of posterior urethral valve and solitary ectopic left kidney was planned for living KTx from a 71-year-old female donor. Laparoscopic left donor nephrectomy was performed and during the preparation of the recipient's right iliac fossa collateral veins were observed which noticed to be thicker than the external iliac vein. A vascular surgery team consultation was made and the iliac vein was



prepared and found to be patent. Operation proceeded with vascular anastomosis of end-to-end internal iliac artery and end-to-side external iliac vein.
Results: Two hours following the transplantation there was oliguria, hematuria and severe patient discomfort. Doppler ultrasonography revealed high resistive index, and no flow on external iliac or transplanted renal vein. The patient underwent immediate exploration and the kidney color was noted purple. RVT was extracted with a venotomy and the patient was let bleeding until the kidney achieved its healthy pink color. Following the coloration of the kidney, transplant nephrectomy was performed immediately, the graft was rinsed with cold UW solution and the kidney was transplanted on the left side. Graft function was delayed and the patient was discharged with serum creatinine level of 2.3 mg/dl.
Conclusion: Preoperative evaluation of external iliac vein with Doppler ultrasonography is important. In case of RVT suspicion, prompt exploration and re-transplantation on the other iliac fossa may be an immediate graft saving decision.

BOS314 TECHNICAL ASPECTS OF UNILATERAL DUAL KIDNEY TRANSPLANTATION FROM EXPANDED CRITERIA DONORS

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Background: One option for using organs from donors with a suboptimal nephron mass, e.g. expanded criteria donors (ECD) kidneys, is dual kidney transplantation (DKT). In adult recipients, DKT can be carried out by several techniques. In this video we are going to show the surgical procedure of unilateral dual kidney transplantation (UDKT).
Methods: The procedure begins with the classic Gibson incision, preferably on the right side. After creating an adequate extraperitoneal space, the right kidney is preferably placed superiorly because its renal vein can be lengthened by a segment of inferior vena cava (IVC), with mechanical stapling of both (upper and lower) openings of the IVC segment; moreover the right kidney has a longer artery. The extended renal vein and renal artery of the right kidney are anastomosed end-to-side to the iliac vessels of the recipient. After revascularization of the right kidney, vascular clamps are placed immediately below the venous and arterial anastomoses. The left donor kidney is transplanted distally, allowing the transplanted right kidney to continue to be perfused The left kidney is positioned inferomedially to the right kidney. The renal artery and vein of the left kidney are anastomosed end to-side to the external iliac vessels. Extravesical ureteroneocystostomies are performed separately, according to the Lich–Gregoir technique, with a double J stent for each ureter.
Results: UDKT can reduce the operating time and surgical trauma in comparison to classical bilateral DKT, leaving the contralateral iliac fossa intact for further transplantation procedures; this technique can be performed using kidneys with multiple arteries and veins and is associated with low surgical complications rate.
Conclusions: Extraperitoneal unilateral positioning of two kidneys from ECD donors through a single Gibson incision is feasible and is not associated with an increased risk to the recipient.

Clinical Liver Surgical technique

BOS315 HEPATIC ARTERY RECONSTRUCTION DURING EX-VIVO NORMOTHERMIC LIVER PERFUSION

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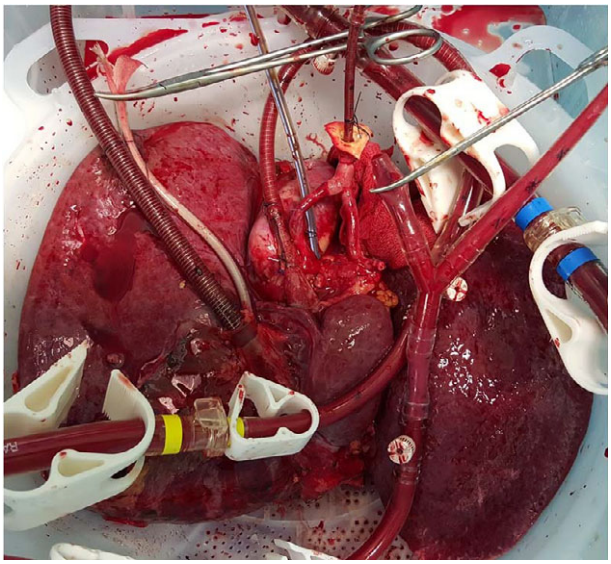
Introduction: Approximately 30% of donor livers will have aberrant hepatic artery (HA) anatomy, with many cases requiring reconstruction either during cold preservation or in situ in the recipient after establishing the main arterial inflow. Normothermic machine perfusion (NMP) involves perfusing a liver with oxygenated blood at 37°C in a heparinised circuit. It also offers a medium where a surgical intervention can be evaluated ex-vivo prior to implantation. We report the first case series of ev-vivo NMP arterial reconstruction.
Methods: As part of the COPE RCT of NMP versus static cold storage in liver transplantation, five livers required hepatic artery reconstruction
which was performed ex-vivo during NMP. The donor and recipient characteristics are reported along with graft outcomes and complications.
Results: A description of the important features of the five cases is shown in Table 1.
There were no cases of cholangiopathy or vascular complications reported at 6 months.
Discussion: Ex-vivo HA reconstruction during NMP is safe, feasible and, from our early experience, does not appear to compromise outcomes or increase the risk of vascular complications. This should represent only the first step in a broader exploration of the potential of ex-vivo NMP surgery.



Donor details				Preservation details		Recipient details				Post-operative details		
Age	Type	ET-DRI	Arterial anatomy	Total pres time (mins)	Details of reconstruction	Age	Cause of liver failure	MELD	*In-vivo* HA anastom time *(mins)*	Peak AST (IU/L)	ITU stay (days)	Hospital admission (days)
72	DBD	2.11	CHA + aRHA from SMA	1167	RHA to GDA	53	PBC	13	28	197	2	7
73	DCD	3.09	aRHA from SMA	685	RHA to SA	58	HCC	9	36	1191	4	9
41	DBD	1.38	aRHA from SMA	469	RHA to SA	39	PCLD	9	40	462	2	5
57	DBD	1.70	aRHA from SMA	1277	RHA to SA	65	HCC	11	52	173	1	7
55	DBD	1.51	aRHA from SMA (cut short)	580	IA to RHA and CHA	43	ALD	21	27	144	7	15

Table 1: Summary of details for ex-vivo arterial reconstruction cases. Key: ET-DRI - Euro-transplant Donor Risk Index; CIT - cold ischaemic time; CHA - common hepatic artery; aRHA - aberrant right hepatic artery; SMA - superior mesenteric artery; SA - splenic artery; GDA – gastroduodenal artery; IA – iliac artery; PBC – primary biliary cirrhosis; HCC – hepatocellular carcinoma; PCLD – poly-cystic liver disease; ALD alcoholic liver disease; MELD – model of end stage liver disease

Clinical Kidney Surgical technique

BOS316 SAFETY OF THE LIVING KIDNEY DONOR: WHAT'S TO BE IMPROVED?

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Background: According to the literature postoperative mortality in living kidney donors is 0.031%. In Italy there have never been reports of post-operative deaths, but there were never carried out systematic reviews on the incidence of non-fatal adverse events and possible consequences.
Methods: We are going to present a video of near misses occurred at our center during a laparoscopic living donor nephrectomy. The living donor nephrectomy at our Center is performed by pure laparoscopic technique. The kidney was already loaded in the bag (Endo Catch™), and then lifted with some stretching of the renal vessels; heparin 5000 UI was administered and a vascular endoscopic GIA stapler was used to divide the renal artery. Then a second vascular endoscopic GIA was prepared to divide the renal vein, but unfortunately due to a mechanical problem the renal vein was sectioned without being sutured.
Results: We have immediately performed a midline laparotomy and we have sutured the renal vein. The following post-operative course of the donor was uneventful; as well as the results for the recipient.
Conclusions: To minimize the risks in living donor donation we have to: (i) set standard of practice; (ii) establish procedures to analyze information (iii) report near misses and disseminate lessons learned

Clinical Liver Surgical technique

BOS317 SAFETY AND RATIONALITY OF EXTRAHEPATIC GLISSONIAN APPROACH FOR LIVING DONOR HEPATECTOMY

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Background: Two major advantages of extrahepatic Glissonian approach are: (i) To minimize dissection and preserve blood supply around the hilar plate in the remnant liver, leading to prevention of bile duct injury (safety), and (ii) To secure maximum margin of hilar structures by determining of the point of bile duct division preceding isolation of vessels (rationality).
Video Presentation: We demonstrate 4 steps of our extrahepatic Glissonian approach for living donor hepatectomy. (i) Isolation of the Glissonian pedicle. After cholecystectomy, the takeoff of the left and right portal branches is confirmed by ultrasound. The right or the left portal pedicle is isolated altogether with the corresponding caudate pedicle with an umbilical tape for a right or a left-sided (left liver, left lateral section, and left liver with Spiegel's lobe) liver graft, respectively. (ii) Identification of hilar structures. Intraoperative cholangiography is performed to identify the point of bile duct division. The artery and portal vein are isolated using vessel loops thereafter and dissected off sufficiently from the hilar plate. (iii) Modified liver hanging maneuver. We apply conventional hanging maneuver for right liver and left liver with Spiegel's lobe grafts. For left liver and left lateral section grafts, the confluence of the middle and left hepatic veins, the plate of Arantius, and the umbilical portion ventral to the plate of Arantius is isolated. A tape is passed through the right and middle hepatic veins, along the Arantius' ligament, and finally to the right of the umbilical portion to accurately set the goal of liver parenchymal transection. After completion of hepatectomy, the tape used for isolation of the umbilical portion is repositioned to secure and divide all caudate pedicles branching from the left portal pedicle. (iv) Division of hilar structures and graft retrieval.
Conclusion: Extrahepatic Glissonian approach for living donor hepatectomy is safe and rational.

BOS318 ESCAPING LIVER TRANSPLANTATION WITH ANTE SITUM RESECTION IN ADVANCED HEPATOBLASTOMA

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Advanced hepatoblastoma (HBL) with tumour thrombi extending into major vessels needs multimodal treatment approaches combining chemotherapy and surgery. Surgical recommendations for pretreatment extent disease (PRETEXT) staging III-IV strongly advocate primary liver transplantation (LT). However, when tumour thrombi infiltrate the inferior vena cava (IVC) and the right atrium, LT might be technically challenging and it is associated with unfavourable survival rates for local recurrence HBL. Therefore, the best surgical approach is not clear and transplant surgeons are exploring technical alternatives.

A 11-months-old boy with serum alpha-fetoprotein (AFP) of 50 795 200 IU/ml and computed tomography showing a right hepatic lobe mass (90 × 78 mm) suspicious of HBL, with tumour thrombi extending from the right hepatic vein into the IVC up to the right atrium, and bilateral lung lesions (PRETEXT III) was referred. After 8 months of chemotherapy (SIOPEL 2004-high risk Protocol), HBL decreased to 61 × 64 mm and lung lesions disappeared, but the tumour thrombi was still present. The child underwent ante situm liver resection: en bloc resection of the extended-right hepatic lobe, retro/suprahepatic IVC, tumoral thrombi extended into the right atrium. The IVC was replaced with fresh aortic graft from blood-group compatible cadaveric donor. During the resection, the remnant liver (SII-III) was perfused through the portal vein with Celsior at 4°C, cooled with ice, and reimplanted by end-to-side anastomosis of the left hepatic vein to the neo-IVC. The post-operative course was uneventful and after 10 months of follow-up the child is in good clinical condition with normal liver function test, AFP of 1.1 UI/ml, free of disease recurrence and with patent aortic graft.

This is the first case of ante situm liver resection combined with hypothermic CPB and IVC replacement for HBL, which is a realistic option to avoid LT for skilled transplant surgeons thanks to the improvement of LT technique.

Clinical Liver Donation and donor types

BOS319 TRANSPLANTATION OF LIVERS RECOVERED AFTER EUTHANASIA: A SINGLE CENTRE EXPERIENCE

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Introduction: Donation after circulatory death (DCD) has increasingly provided organs for liver transplantation (LT) and in our country includes donation after euthanasia (also referred to as DCD-V). The explicit wish for organ donation was expressed by the donors after request for euthanasia was granted according to the Belgian legislation codified in 2002. We report the results after LT from euthanasia donors in our center.
Methods: All donors suffered unbearable suffering from a non-malignant disease. In accordance with ethical guidelines, euthanasia and LT were clearly separated. Euthanasia was performed adjacent to the operating room by treating physicians not involved in the transplant process and in the absence of the procurement team. Continuous data are presented as median (IQR).
Results: Between 1/2009 and 12/2015, 94/409 (22%) DCD-LT were performed, of which 11 (11.7%) were DCD-V LT. Euthanasia donors (6 M, 5 F) aged 44 years (33–62). Eleven recipients (6 M, 5 F) aged 65 years (52–68), underwent DCD-V LT for hepatocellular carcinoma ($n = 2$), Budd Chiari ($n = 1$), acute liver failure ($n = 1$), post-NASH ($n = 2$), post-ethyl ($n = 2$), post-hepatitis B ($n = 1$), cryptogenic ($n = 1$), and primary biliary cirrhosis ($n = 1$), with a labMELD score of 19 (12–26). Donor agonic [1 (1.5–5)] and total warm ischemia [12 minutes (10–15)] were short, and cold ischemia minimal [4.5 hours (4–7)]. Early graft dysfunction occurred in one DCD-V LT, two recipients experienced acute kidney injury. Hospitalization was 16 days (14–18). One patient developed non-anastomotic biliary strictures 2 months after DCD-V LT. Two recipients died due to sepsis and one for recurrent hepatocellular carcinoma. Patient survival at 5 year was 71.6%, and death-censored graft survival was 87.5% [follow-up 6.4 year (95% CI: 5.5–7.4)].
Conclusions: Honoring the last desire of patients granted euthanasia accounted for 11% of our DCD LT with favorable early outcome and recipient survival.

BOS320 SIGNIFICANCE OF PROPER GRAFT SELECTION ON ADULT LIVING DONOR LIVER TRANSPLANT RECIPIENTS WITH PREOPERATIVE DETERIORATED CONDITION

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Background: The outcome of living-donor liver transplantation (LDLT) is poor for recipients with severely deteriorated preoperative condition. This study therefore evaluated the proper graft selection according to the recipients' preoperative condition.
Methods: We evaluated the clinical outcomes in 70 patients who underwent adult LDLT from October 2003 to June 2016 in our institution, excluding ABO incompatible cases. Preoperative risk factors included MELD score >20, preoperative hospitalization for over 2 weeks or intensive care unit admission and infection within 1 month before LDLT. Patients were classified into those with 0–1 (Group LR, $n = 46$), 2–3 risk factors (Group HR, $n = 24$).
Results: The 1-year overall survival (OS) rate after LDLT was significantly lower in Group HR (79.8%) than in Groups LR (93.3%) ($p = 0.004$) (Figure 1). In Group LR, OS rates did not differ significantly by graft type or donor age. In Group HR, OS rates at 1 (94.4% vs. 66.7%), 3 (94.4% vs. 50%) and 5 (76.3% vs. 25%) years were significantly higher using right ($n = 18$) than left ($n = 6$) lobe grafts ($p = 0.045$) (Figure 2).
Conclusion: Proper graft selection is very important to improve the outcome of LDLT recipients in deteriorated preoperative condition. LDLT using right lobe grafts may be recommended for the severely deteriorated patients with high risks.

Figure 1

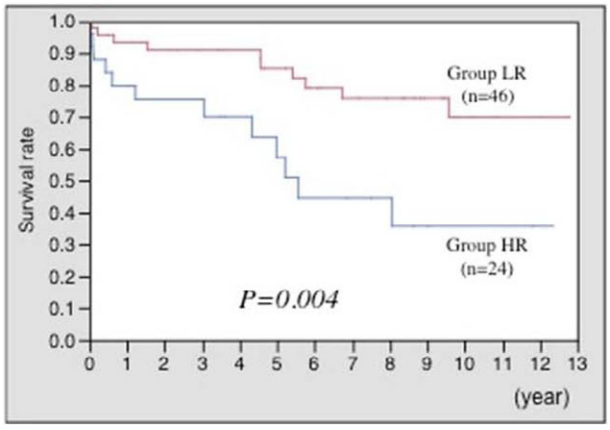
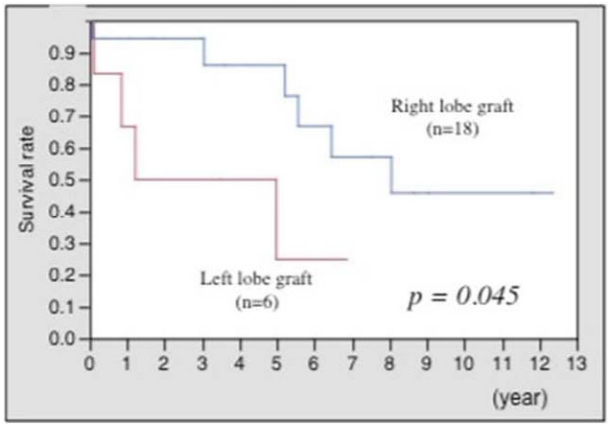


Figure 2



BOS321 GRAFT SELECTION STRATEGY IN ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION: WHEN BOTH HEMI-LIVER GRAFTS MEET VOLUMETRIC CRITERIA

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Background: To ensure donor safety in living donor liver transplantation (LDLT), the left and caudate lobe (LL) is the preferred graft choice. However, patient prognosis may still be poor even if graft volume selection criteria are met. Our aim was to evaluate the effects of right lobe (RL) donation when LL graft selection criteria are met.
Method: Consecutive donors ($n = 135$) with preoperative LL graft volumetric graft volume/standard liver volume (GV/SLV) ≥35% and RL remnant ≥35%, were retrospectively studied. Patients were divided into two groups: LL graft and RL graft.
Results: Recipient's body surface area, model for end-stage liver disease score and donor's age were higher in the RL group. Donor's body surface area and preoperative volumetric GV/SLV of the LL graft were smaller in the RL group. The predicted score (calculated using data for graft size, donor age, model for end-stage liver disease score and presence of portosystemic shunt, which correlated well with graft function and with 6-month graft survival) of the RL group was significantly lower if the LL graft were used, but using the actual RL graft improved the score equal to that of the LL group. Six-month and 12-month graft survival rates did not differ between the two groups. In patients with a poor prognosis, a larger RL graft improved the predicted score and survival was equal to that of patients who received LL grafts.
Conclusion: Our strategy was to first select the LL graft, and then use the larger RL grafts for patients who were expected to have a poor prognosis if the LL graft would have been used. This strategy improved the predicted score, and as a result, the prognosis after LDLT was not different between patients with LL grafts and RL grafts. Graft selection not only by GV but by donor age and recipient MELD score would also improve outcomes after LDLT.

BOS322 LIVER TRANSPLANT USING LIVING DONORS WITH SICKLE CELL TRAIT

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Background: Living donor liver transplant (LDLT) is an important source of organs particularly with the cadaveric organ shortage. It is the main source of liver transplant in the East (Korea, Japan, and Saudi Arabia). At our program, 63.6% of liver transplant were performed from LDLT (599 out of 941).

Donor safety is the main focus of donor evaluation, but a balance is needed to avoid unnecessary exclusion of donors. There is limited data on the safety of use of living liver donors in patient's sickle cell trait. We used to exclude donors with sickle cell trait but we started accepting them since 2012. We report the donor safety of 7 patients with sickle cell trait.
Method: This is a retrospective chart review of living liver donors from January 2012 until September 2016, seven donors identified. The medical records were reviewed for age, gender, relation to the recipient, Body mass index (BMI), blood group, history of preoperative blood transfusion to decrease

	Age	Gender	BMI	Relation	Blood Transfusion	Blood Group	Hb	MCV	Hb S	Hospital stay (days)	Complication
1	27	Male	24	Father	No	A	14	82	35.3	5	none
2	36	Female	31.3	Mother	Yes	B	12	72	32.8	5	Peri-hepatic fluid collection
3	24	Male	21.6		No	A	12.2	59	21.2	5	Hypertrophic scar
4	26	Male	20		Yes	O	16	78	36	6	none
5	28	Male	23.5	Father	No	O	14.4	64	24	4	none
6	32	Male	28	Uncle	No	O	15.7	68	25	4	Hypertrophic fluid collection
7	38	Female	29	Mother	No	O	11.3	69	27	5	Pelvic fluid collection

Hemoglobin S (Hb S), Hemoglobin level (Hb), Mean corpuscular volume (MCV), Hemoglobin S level, hospital stay and complications.
Results: Out of seven donors, five males and 2 females, age between 24–38 (mean 30), the donors were father (2), mother (2), or uncle (3), all donors donated left lateral segment (LLS) to a pediatric recipients, Hb level ranged from 11.3 to 16 (average 13.6), MCV ranged from 59–84 (70.3), Hb S level ranged from 21.2 to 36 (28.7), hospital stay from 4–6 days (average 4.8 days)

Two patients received blood transfusion 2 days prior to surgery and their Hb S level decreased from 32.8 and 36 to 27.5 and 30.6 respectively.

All other patients donated blood 2 days before surgery and were well hydrated the day of surgery.

No immediate or long term complication related to the surgery or sickle cell trait.
Conclusion: Liver donation is safe from sickle cell trait donors as long as dehydration is avoided and oxygen saturation is maintained normal throughout surgery.

BOS323 THE OUTCOME OF LIVING DONOR DOMINO LIVER TRANSPLANTATION USING FAMILIAL AMYLOID POLYNEUROPATHY GRAFTS

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Background: Domino liver transplantation using familial amyloid polyneuropathy (FAP) has been significant for the expansion of potential donor. In this study, the short and the long-term outcomes of domino liver transplantation using grafts taken at the living donor liver transplantation for FAP patients were investigated on the surgical complications and de novo amyloid neuropathy in a single institution.
Methods: From May 2003 to January 2017, 25 patients (18–62 years old) received grafts from FAP patients (25–52 years old) as the living donor domino liver transplantation (LDDLT).
Results: Indications in domino recipients were HBV cirrhosis ($n = 4$ w/HCC, $n = 2$ w/o HCC), HCV cirrhosis ($n = 3$ w/HCC, $n = 3$ w/o HCC), alcoholic cirrhosis ($n = 3$), re-transplantation ($n = 4$) and others ($n = 6$). All but one of LDDLT recipients were implanted with whole liver. FAP livers were resected without retrohepatic inferior vena cava and this caused multiple orifices of the hepatic vein in the graft. In 22 cases, two or three orifices were reconstructed. Portal vein (PV) in all cases except two was simply anastomosed in an end-to-end fashion. All the domino grafts had multiple hepatic arteries (HA). In 15 out of 25 cases, only the right hepatic artery was anastomosed, and the other arteries were left non-reconstructed. Duct-to-duct biliary reconstruction was performed in 18. There were no post-transplant complications of HA, whereas HV stricture was detected in two cases and PV thrombosis was in one case. Incidence of biliary stricture was 20% ($n = 5$). Development of de novo amyloid polyneuropathy was detected in five cases (20%), and the shortest period to the onset was only 6 years. The 1 and 5-year patient survival was 82.9 and 72.5%
Conclusions: LDDLT using FAP grafts have acceptable outcomes despite the complicated surgical technique. However, development of de novo amyloid polyneuropathy can be possible even after relatively short period from the transplant.

Basic Liver Donation and donor types

BOS324 FRENCH LIVER DONOR RISK INDEX

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Context: In a context of organ shortage, transplantation with an organ coming from extended criteria donor (ECD) is more frequent. Liver donor risk indexes (LDRI) have been developed to predict graft failure associated with donor characteristics but they are not applicable in France because donors differ from those used to establish them.
Objective: The objective of this study was to determine donor characteristics associated with 1-year liver graft failure in France and build a French LDRI.
Method: Using the French registry CRISTAL, we included all adult recipients transplanted between 2007 and 2013 and their donors ($N = 5759$). Study endpoint was 1-year post-transplant graft failure (recipient death or retransplant). Survival rates were estimated using the Kaplan-Meier method. Cox models were used for multivariate analysis and to construct the French LDRI (FLDRI).
Results: 31% of donors were aged 65 years or over and 44% were women. Cause of death was stroke in 61% of cases, head trauma in 24% and anoxia in 11%. Hypertension and GFR<60 were reported in respectively 36% and 34% of cases. Donor factors associated with 1-year graft failure were: age >65, Hypertension, death due to stroke, low GFR and height. Significant recipient factors included in the model were: Age, intensive care unit/intubation, indication, GFR/dialysis, viral C cirrhosis. The predictive accuracy of the model with recipient and donor factors adjusted for cold ischemia was good (concordance probability estimation = 0.7). The highest FLDRI quartile had a 1-year survival of 78.6% whereas the lowest had 86.3%. Low and high-risk recipients receiving a graft from a high-risk donor had 1-year graft survival of 87.5% and 63.0% respectively versus 89.9% and 78.4% for a low risk donor.
Conclusion: The highest FLDRI quartile had lower 1-year graft survival. The FLDRI could help provide a better matching with recipient and increase procurement and survival of ECD graft.

Clinical Liver Donation and donor types

BOS325 DECISION AMBIVALENCE IN DIFFERENT TYPE OF POTENTIAL LIVING LIVER DONORS DURING ASSESSMENT

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Background: Living liver donor should careful assess for their willingness as well as the voluntary before the surgery. The purpose of this study was to explore the decision ambivalence in different type of potential living liver donors during assessment period.
Method: A cross-sectional and correlation study was conducted. One hundred and thirty-three actual living liver donor with 206 potential living liver donors divided into 4 groups (the self-decline group ($n = 20$), the not-selective group ($n = 63$), the recipient condition group ($n = 68$), and the candidate condition group ($n = 35$)) were include in this study.
Results: The mean score of ambivalence (possible score range 0–7) of total participants was 4.23 (SD 1.88). The ambivalence of the self-decline group was highest. It was higher than the actual group (5.55 vs. 3.83) and the not-selected group (5.55 vs. 3.92). There was 50% of candidates in the self-decline group feel relieve if they could not donate, but there was only 9.8% in the actual group ($\chi^2 = 23.11$, $p < 0.0001$); 75% of self-decline group though the decision was hard to make, significant higher than actual group (38.4%) ($\chi^2 = 15.5\%$, $p = 0.005$); 90% of self-decline group agree that they did not want to donate even if someone else could not ($\chi^2 = 19.53$, $p = 0.001$); 95% self-decline group feel unsure about donating, it was also significant higher than the actual group (51.5%) ($\chi^2 = 17.96$, $p = 0.001$).
Conclusion: In general, ambivalence was common in potential living liver donors even the actual donor. It was not an all or none phenomenon. Candidates who self-decline from assessment experienced obvious ambivalence about donation. We suggested that a summary score higher than 4 may be a meaningful score in the Ambivalence Scale. We also suggest clinician use the content of the Ambivalence Scale to understand the ambivalence experience of decision-making of living liver donor candidates deeply.

BOS326 LAPAROSCOPIC APPROACH FOR LIVING DONOR TO PAEDIATRIC LIVER TRANSPLANTATION: EXPERIENCE OF THE FIRST 5 CASES IN SPAIN

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Introduction: Our paediatric liver transplantation program started on 1990 and at present, has performed more than 170 children's liver transplants. In the last year, laparoscopic approach was first used. Five cases of living donor with laparoscopic approach were performed in 4 months; one of them was an auxiliary liver transplant.
Objectives: In this study we report our series of five cases of living donor liver transplantation (LDLT) performing left lateral sectorectomy with a pure laparoscopic approach.
Results: Five pure laparoscopic LDLT from March to June 2016 were performed. The average age of donors was 32.4 ± 3.9 years. The mean BMI of the donors was 22.8 ± 3.9. 60% were ASA I and 40% ASA II. Pre-tx liver function was normal in all donors. Only two donors required Pringle maneuver (3 and 2 cycles respectively – 30 and 25 min each one). The mean age of the recipients was 3.2 ± 4.9 months with an average weight of 12.6 ± 10.5 kg. The aetiology was biliary atresia in 3 of them and metabolic disorders in the other two. In one case, an urgent transplant was performed due to worsening of the liver function of the recipient. The surgical time of donor surgery was 386 ± 25.1 minutes and the recipient's time was 439 ± 87.5 min. The warm ischemia time (WIT) was 9.2 ± 3.5 minutes; cold ischemia time was (CIT) 85.2 ± 12.5 minutes. The conversion rate was 0%. The CCI of the donors was 0. The recipient CCI of our series was 15.1 ± 14.7; with a case that required intervention (auxiliary case) with general anaesthesia for portal flow re-modulation. The mean stay of the recipients was 22.8 ± 7.9 days and the

donors was 4.4 ± 1.5 days. Perioperative donor and recipient mortality was 0%. To date with a mean follow-up of 6.8 (9–6) months, our series has a survival rate of 100% and a recurrence rate of 0%.
Conclusions: We can propose the laparoscopic approach in reference centers as "gold standard". Minimally invasive approach to living donor can be considered a safe and effective procedure.

BOS327 COMBINED LIVER-KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Renal dysfunction is a common association with advanced liver failure. The proportion of patients with advanced chronic kidney disease and need for liver transplantation has increased in the last years and for these patients the best option is the combined liver-kidney transplant (CLKT). We have been performing CLKT since 1993 in our center. In this study we analyzed the evolution of the CLKT program in our hospital.
Methods: We analyzed all CLKT performed in Hospital Clinic between May 1993 and August 2016. We studied demographic and clinical variables. Survival analysis was performed by Kaplan-Meier method.
Results: In the study period, 82 CLKT were performed.

62% of the recipients were men and 38% female. The mean age was 48.5 ± 10.5 years.

The mean donor age was 39.09 ± 13.28. Cause of death was: Cerebral Vascular Accident in 56.1% of the donors, Cranial Trauma in 29.3% and Anoxic Encephalopathy in 14.6% of them.

The recipients renal disease etiology was: Chronic Glomerulonephritis in 30.5%, Polycystic disease (PD) in 28%, Chronic Interstitial Nephropathy in 8.5%, Diabetes Nephropathy in 7.3%, Primary Hyperoxaluria (PH) in 7.3%, IgA nephropathy in 3.7%, Amyloid Disease (AD) 8 in 3.7%, calcineurin inhibitor toxicity in 3.7%, Hemolytic Uremic Syndrome in 2.4% and Acute Tubular Necrosis in 4.9%.

The main causes of liver disease were: hepatitis C virus (39%), Polycystic disease (22%), alcoholism (17%), PH (7.3%) and AD (3.7%). Mean patient survival time was 168.54 ± 12.40 months. No significant difference was found in survival analyzed by liver or kidney disease. 24.4% of the recipients presented liver decompensation, and 17.1% presented complications derived from PD. Mean kidney graft survival was 148.89 ± 12.49 months.

Our results of CLKT showed acceptable outcome not only for patient survival but also for kidney graft survival. CLKT is the best alternative to consider in candidates for liver transplantation with chronic kidney disease.

BOS328 RIGHT POSTERIOR SEGMENT GRAFT IN ADULT LIVING DONOR LIVER TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Background: To clarify the background of donor and recipient in the case which we selected posterior segment graft in adult living donor liver transplantation (LDLT).
Methods: Between December 1998 and Jun 2016, 309 adult patients underwent LDLT and posterior segment graft was selected in 9 (2.9%) cases in Kumamoto University Hospital. The background, operative variables, and postoperative courses of the donor and recipient were evaluated retrospectively.
Results: In the donor operation, the mean volume of bleeding and operative time was 7.1 ml/kg, 482.7 minutes respectively. The mean hospitalized period was 23.1 days and there were no complications after the operation.

In the recipient operation, the mean volume of bleeding, operative time, cold ischemic time, warm ischemic time and graft-recipient body weight ratio (GRWR) was 101.3 ml/kg, 768.6 minutes, 82.9 minutes, 48.9 minutes, 0.83% respectively. The mean hospitalized period after LDLT was 66.2 days and biliary stent tube was inserted for biliary anastomotic stricture as the postoperative complication in 4 cases (44.4%). The primary disease of the recipient was primary biliary cirrhosis (PBC) in 3 cases, viral cirrhosis in 3 cases, alcoholic cirrhosis in 1 case, idiopathic cirrhosis in 1 case, familial amyloid polyneuropathy (FAP) in 1 case. The overall 1-, 3-, and 5-year recipient survival rate was 77.8%, 77.8%, 77.8% respectively. Two recipients were dead for severe rejection in 12 days after LDLT, and the rupture of hepatic artery pseudoaneurysm 8 months after LDLT. Retransplantation from deceased donor was performed for graft failure 3 years after primary LDLT in one case.
Conclusions: In the LDLT with right posterior segment graft, donor operation was performed safely. Further consideration and pre- and post- operative evaluation would be necessary to prevent biliary anastomotic stricture in recipient operation.

Clinical Others Donation and donor types

BOS329 THE MEANING OF BEING A LIVING DONOR (KIDNEY, LIVER AND STEM-CELLS) – A META SYNTHESIS

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Background: All live donors are in a similar situation, despite donating an organ or stem-cells. Potential donors go through several tests, medical and psychosocial assessments. Donors are giving something from their own body, to somebody else in great need for survival or to get the best available treatment. Studies on living donors' experiences have been kept apart; experiences of stem cell donors, kidney donors and liver donors have not been explored in the same studies. The aim of this study was therefore to synthesize the meaning of being a live donor of a kidney, a liver part or stem-cells.
Methods: After a literature search 150 qualitative potential studies from 1968–2015 were found and 38 of these were selected. In the analysis, we followed the steps of meta-ethnography as described by Noblit & Hare (1988). For transparency in reporting synthesis of qualitative research, the ENTREQ statement by Tong et al. (2012) was used.
Results: Together the studies included more than 500 donors and were mainly conducted in Anglo-Saxon countries ($n = 24$). The range of time since donation varied from 2 days to 29 years. The most commonly used qualitative method was phenomenology ($n = 15$). The majority of the studies were with living kidney donors ($n = 23$). Six themes, including both positive and negative experiences, were revealed from the synthesis, showing a deeper understanding of what it means to be a donor; You do what you have to do, Solitariness & Abandonment, Suffering, Pride & Gratitude, Sense of togetherness and A life changing event.
Conclusion: This synthesis concludes that the motives for donation are directed by the relationship between the donor and the recipient. It is that you donate something from your body that is important, not what you donate. Live donation is a life-changing event, with a clear before and after.

Clinical Liver Donation and donor types

BOS330 COMPARATIVE STUDY OF PURE LAPAROSCOPIC LIVING DONOR RIGHT HEPATECTOMY VERSUS CONVENTIONAL OPEN LIVING DONOR RIGHT HEPATECTOMY

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Introduction: To compare the outcomes of pure laparoscopic living donor right hepatectomy (LLDRH) *versus* conventional open living donor right hepatectomy (OLDRH).
Methods: All consecutive cases of LLDRH between November 2014 and January 2017 in a tertiary referral hospital and 1:2 case matched OLDRH during same period were enrolled in this retrospective cohort study. All surgical procedures were performed by one surgeon. The LLDRH and OLDRH groups were compared in terms of donor demographics, preoperative data, clinical perioperative outcomes, and recipient perioperative outcomes.
Results: LLDRH group ($n = 20$) had a significantly shorter postoperative hospital stay than the OLDRH group ($n = 40$) (7.8 ± 1.8 vs. 11.1 ± 2.4 days, $p < 0.001$) and less intravenous pain medication than OLDRH group (2 (0–6) vs. 6 (0–8) vials, $p = 0.016$). In LLDRH group, there was no post operative complication such as transfusion, wound infection, or bleeding. Furthermore, there was no open conversion during LLDRH procedure.
Discussion: LLDRH was a safe and feasible procedure for selected donors. It required shorter hospital stay and resulted in less analgesic requirements. The authors suggest that LLDRH could be a reasonable operative option for selected donors.

Clinical Kidney Histocompatibility

BOS333 SIGNIFICANCE OF C3D BINDING DONOR SPECIFIC ANTIBODIES PERSISTING SHORT TERM AFTER KIDNEY TRANSPLANTATION

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Background: Antibody-mediated rejection (AMR) is a major cause of renal graft dysfunction. Complement binding ability of donor specific antibody has been suggested as a better predictor of AMR, thus more reliably stratify the risk of graft dysfunction. Here, we've questioned the significance of donor specific antibodies (DSA) persisting until 4 weeks after kidney transplantation (KT) in the aspect of complement binding or not.
Methods/Materials: We studied the sera from 71 patients including 60 with pre-existing DSA and 11 with *de novo* DSA (*dn*DSA), which collected at pre- and post -1 and -4 week transplantation for the ability to bind C3d using flow bead assays.
Results: Among 131 sera, 35 (27%) were positive for C3d assay. Thirty-six (17.8%) among 202 DSAs showed C3d binding activities (C3d+) and Class II DSA accounted for 91.5% of them. MFIs of single antigen bead assay (SAB) of the C3d+ DSAs were significantly higher than the C3d- DSAs (median 10,108 vs. 2,589, $p > 0.05$). The lowest MFIs of DSAs showing C3d binding activities were 5,047 for Class I and 4,401 for Class II. Frequencies of pre-transplant C3d+ DSAs between patients with and without rejection episodes were not different (33.33% vs. 37.5%). However, 4 out of 10 patients who had had persistently C3d binding DSAs after KT experienced acute rejection compared to one out of 5 patients who had not. Also, two out of 4 *dn*DSA+ patients who experienced acute rejection had C3d+ DSAs but none of 3 patients without rejection had C3d+ DSAs.
Conclusion: The C3d binding activities were closely paralleled by the increased MFI of single antigen bead assay. The presence of persistently C3d binding DSAs even after pretransplant conditioning and of C3d binding *dn*DSA seemed to be useful to stratify the risk of rejection in kidney transplantation.

Clinical Heart Histocompatibility

BOS334 HLA-DR MISMATCH IMPACTS LONG-TERM MORTALITY AFTER HEART TRANSPLANTATION

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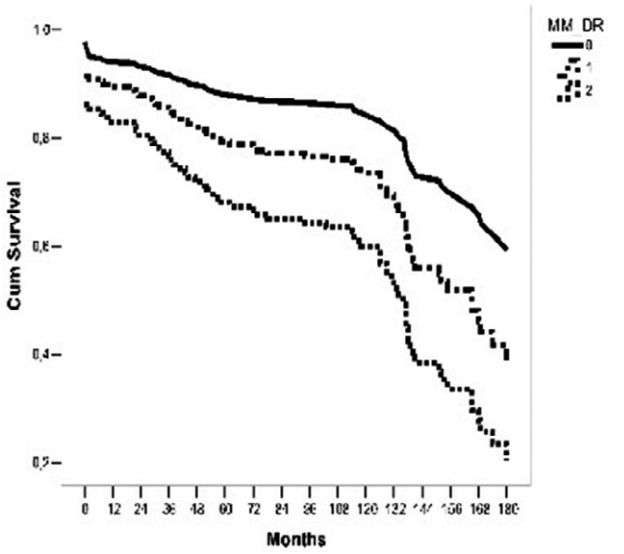
Objectives: The role of HLA matching on the prognosis of heart transplantation is still unclear and at the moment is not considered as measure to of organ allocation. We previously demonstrated an association between DR-mismatch on in hospital mortality. Aim of the study is to evaluate the impact of human leukocyte antigen matching on long-term outcome after heart transplantation.
Material and Methods: We evaluated the HLA mismatch on long term mortality of 158 consecutive patients that underwent heart transplantation from 2000 to 2008 with a minimum follow-up of 10 years. HLA-A, -B and -DR were determined by means of serological and molecular techniques. Univariate analysis and a multiple logistic regression model evaluated the effect of HLA variants on mortality independently of clinical variables.
Results: Mortality after a mean follow-up of 107.7 ± 59.4 months was 49.4%. Univariate analysis demonstrate in deceased heart transplanted patients higher donor age (34.9 ± 13.2 – $p = 0.036$), HLA-DR mismatch (1.45 ± 0.6 – $p = 0.024$) and previous cardiac surgery (29.5% vs. 16.3% – $p = 0.047$). A lower mortality was observed in female (30.3% vs. 54.4 – $p = 0.014$), No statistical differences were found for recipient age, mismatch sex, mismatch HLA-A and HLA-B, AKI, ischemia duration, and perioperative level of troponins. In Cox regression analysis HLA-DR mismatch predict mortality (HR = 1.691 – 95% CI 1.131–2.526; $p = 0.010$), independently by the effect exerted by covariates such as recipient sex, recipient age, mismatch HLA-A and HLA-B and previous cardiac surgery.
Conclusions: HLA-DR mismatch predicts long term survival in heart transplantation.



Clinical Liver Histocompatibility

BOS335 PREVALENCE AND IMPACT OF HLA ALLOANTIBODIES IN LIVER TRANSPLANTATION IN THE 1ST AND 5TH YEAR A SINGLE CENTER EXPERIENCE

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Background: The significance of humoral response for allograft survival after liver transplantation (LT) is still a matter of debate. The aim of this study was to investigate the prevalence and impact of the pre- and post-LT HLA alloantibodies in the 1st and 5th year.
Methods/Materials: A total of 77 primary liver only transplant patients (2010–2016) were tested for HLA alloantibodies, with single antigen bead technology, before and 1, 6, 12 months after transplantation and thereafter annually. HLA typing was performed for all donor-recipient pairs. Statistical analysis was performed through IBM SPSS version 19 using *t*-test, chi-square and Fisher's exact test at a level of $p < 0.05$.
Results: Preformed HLA alloantibodies (PA) were detected in 40.4% of patients who had 57.1% and 42.9% one and five year survival rate respectively, vs. 80.6% and 77.4% in patients negative for PA ($p = 0.066$ and $p = 0.01$) respectively. Only 9.6% of these patients had pre-existing donor specific antibodies (DSA) class I or II with no important statistically difference in one- and 5-years survival rate. In 7.7% and 1.9% of patients PA class I and II were maintained after LT with 50.0% in 1- and 5-years survival rate vs. 72.9% and 64.6% in negative patients respectively. 40% of patients developed de novo HLA alloantibodies after LT and 22.2% de novo DSA (3 class I and 9 class II). The difference in graft survival rate between de novo DSA positive and negative patients was not statistically important may be due to small number of transplanted patients with de novo DSA.
Conclusion: Preformed HLA alloantibodies are common in LT recipients. Patient and graft survival rate seemed to be affected by preformed anti-HLA antibodies and PA maintained after LT but not by de novo DSA, although independent validation is needed. Long-term outcome in patients with post-transplant DSA needs further study.

Clinical Kidney Histocompatibility

BOS336 STRATEGIES ENABLING CROSS-MATCH POSITIVE PAEDIATRIC HLA-ANTIBODY INCOMPATIBLE RENAL TRANSPLANTATION

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Background: End stage renal disease diagnosed soon after birth results in initiation of dialysis in early childhood. Maintaining good access for dialysis in small children is challenging and urges prompt transplantation. Proportion of waiting-list children sensitized due to failed transplant is growing. An alternative is an HLA-antibody incompatible (HLAi) transplantation from a living donor.
Methods: Having established desensitization protocol enabling paediatric cross-match positive renal transplantation we carefully consider this option for highly sensitized children. Desensitization is based on a test plasma exchange that allows estimating a number of sessions required to achieve negative cross-match. Induction immunosuppression is with T-cell depleting agent. Monitoring of anti-HLA antibodies is frequently performed with Luminex single-antigen bead assays.
Results: Previously we reported an HLAi living donor renal transplantation in two highly sensitized children (14-year-old girl and a 13-year-old boy) with calculated reaction frequency (cRF) of 100%. After 2 years of follow-up both have stable renal allograft function. Last year two 8-year-old boys received kidneys from their relatives to whom they had donor specific antibodies (DSA). Level of DSA was fluctuating over time and cRF ranged between 50 and 90%. Both patients have stable graft function four months after their transplants.
Conclusions: Sensitization with a broad-spectrum of anti-HLA antibodies as a result of previous transplant is an increasing problem. It precludes early deceased donor transplant and matching in a pair exchange programme. Tailored desensitization based on test plasma exchange allows planning of optimal strategy to safely proceed with transplant surgery. Due to fluctuating nature of DSA, in selected cases the kidney transplant from cross-match positive donor is possible without antibody removal providing careful immunological monitoring.

BOS337 PRE-EXISTING ANTIBODIES IN KIDNEY TRANSPLANTATION

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It is well known, that lower PRA score is associated with higher transplant survival rate. Sometimes a fall in PRA at the point of transplantation compared to the peak value may lead to an underestimation of the risk.

144 recipients from the waiting list, with anti-HLA antibodies I, II or both classes (PRA > 5%) were included in the study. Patients were screened periodically to identify PRA and the specificity of antibodies. Of these recipients, 86 received a kidney transplant. At the point of the transplantation the patients had no donor specific antibodies. Antibodies were analysed/studied using the Luminex platform (single antigen-bead based assay).

In the patients on the waiting list, the PRA, as well as MFI of circulating antibodies were not constant in time. Current PRA may decrease over time to 30–40% of the historical peak PRA. This is accompanied by a marked reduction in the MFI of some antibodies – sometimes below the lower threshold, which in this case was 1000. At times this may lead to an underestimation of the immunological risk.

In univariate model, the increase in current PRA, increase in historical peak PRA and a decrease in ΔPRA (difference between peak and current PRA) was associated with an increased risk of humoral rejection ($p < 0.0001$ each) and transplant loss ($p < 0.001$ each). ΔPRA is a very ambiguous measure. The inclusion of ΔPRA in the multivariate model of proportional Cox risks shows that an increase in current PRA is associated with increased risk of humoral rejection ($p < 0.001$), but not with transplant survival ($p = 0.067$). Whilst historical peak PRA remains a significant factor for both humoral rejection of the transplant ($p < 0.001$) and for its survival ($p < 0.001$).

In the selection of donor-recipient pairs it is necessary to consider the spectrum of antibodies at the point of the highest PRA score. A reduction in this indicator may in some cases be hiding antibodies, which are reactive to donor antigens or to certain epitopes.

Clinical Others Histocompatibility

BOS338 IGG SUBTYPES IDENTIFIED BY A FLOW CROSSMATCH ASSAY INCREASES SUCCESSFUL TRANSPLANTS IN SENSITIZED RECIPIENTS

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Introduction: A flow cytometric crossmatch (FCXM) is the final test determining donor-recipient compatibility. Positive FCXM result contraindicates a transplant. A standard FCXM assay cannot discriminate between the various subtypes of the immunoglobulin molecule (IgG1, IgG2, IgG3, and IgG4). We have developed a new FCXM assay that distinguishes between harmful complement-activating (IgG1 and IgG3) and non-complement activating (IgG2 and IgG4) antibodies using donor cells and recipient sera. Our new FCXM assay has led to successful heart and kidney transplants.
Methods: PBMCs isolated from the donor samples were incubated with the pre-transplant sera from 8 heart, and 10 kidney recipients. The cells were then incubated in the lyophilized custom cocktail of antibodies that specifically recognize the various IgG subtypes bound to the cells, followed by FCXM analysis. C1q testing was carried out on all sera.
Results: *Heart*

Most of the heart transplant cases studied had a positive crossmatch due to IgG2 or IgG4 antibodies correlating with C1q results. Two cases were positive for C1q; probably due to prozone effect. All cases had positive 30-day and 90-day survival post-transplant with no PGD or >2R rejection. Two cases with documented AMR continued to have normal graft function.

Kidney

There was almost complete agreement between the IgG subtype assay and C1q assay results in most of the cases studied. A positive FCXM was due to presence of non-complement activating IgG 2 or IgG4 antibodies. Only one case showed the presence of IgG3 antibodies with a negative C1q; probably the result of denatured antibodies.
Conclusion: Our results demonstrate that our assay facilitates safe transplants even in the presence of a positive FCXM. The assay has shown itself to be accurate in detecting the IgG subtype/s causing a positive FCXM. Clinical implementation of our assay would have a great impact on increasing the number of successful transplants.

Clinical Kidney Histocompatibility

BOS339 THE IMPACT OF TRANSPLANT NEPHRECTOMY AND IMMUNOSUPPRESSION CESSATION ON HLA SENSITISATION: A RETROSPECTIVE ANALYSIS

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Background: The development of HLA antibodies towards a failing renal allograft impacts upon chance of future transplantation. We assessed the formation of HLA antibodies in patients who underwent transplant nephrectomy at our centre over a 10 year period.
Methods: We conducted a retrospective study evaluating patients with a failed transplant who underwent graft nephrectomy between 2005 and 2015. Samples were tested for donor specific antibodies at 5 time points: pre-nephrectomy, post-nephrectomy, pre-immunosuppression (IS) weaning, post-IS weaning and post-IS cessation. Calculated reaction frequency (cRF) was determined for each time point and entered into the ODT chances of transplant (CoT) calculator.
Results: 24 patients (14 male, mean age 45 years) had sufficient data for analysis. Mean time from immunosuppression weaning to nephrectomy was 376 days, and from nephrectomy to immunosuppression cessation 166 days. One patient had no sample post-immunosuppression cessation. One patient remained on immunosuppression throughout. 7 patients had immunosuppression stopped within 14 days of nephrectomy. The table below shows cRF and chance of transplant at specified time points.

	Mean cRF (%)	Chance of transplant at 5 years (%)
Nephrectomy		
Pre-Nephrectomy	58	46
Post-Nephrectomy	69	46
Immunosuppression		
Pre-IS wean	31	54
Post-IS wean	69	46
Post-IS cessation	89	42

Discussion: This analysis investigated changes to sensitisation and chance of future transplant after nephrectomy and immunosuppression withdrawal. An increase in cRF following nephrectomy and stepwise increase in cRF as immunosuppression was withdrawn was observed. Immunosuppression changes occur in close time proximity to transplant nephrectomy which confounds this assessment however it is clear the risks and benefits of stopping immunosuppression need to be carefully considered on an individual basis to maximise chance of future transplant.

BOS340 DSA STRENGTH ASSESSMENT IMPROVES RISK STRATIFICATION IN KIDNEY TRANSPLANTATION

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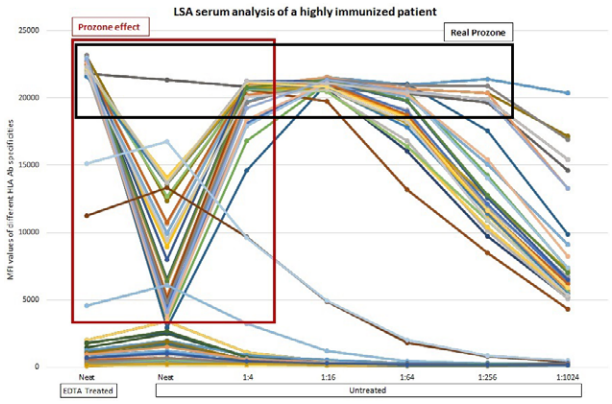
Background: With the recognition that not all DSA detected by Luminex single antigen assay (LSA) are detrimental, a challenge in kidney transplantation (TX) is to identify DSA associated with poor graft outcome. MFI values are often used to evaluate the impact of DSA, but the clinical significance of absolute MFI remains unclear.
Methods: In our single center study, we prospectively collected data on 676 patients (pts) who underwent kidney TX between 2011 and 2016. HLA antibodies (abs) were prospectively measured by LIFECODES® LSA but re-interpreted for this study. Ab specificity and strength were then integrated with the clinical database. Finally, for a highly sensitized pt, the HLA abs MFI of EDTA-treated serum was compared with the MFI of different dilutions of untreated serum.
Results: Among the 676 pts, 31 (4.6%) were transplanted with pre-TX DSA, while only 7 pts (1.0%) developed de novo DSA (DN DSA). Ten (29.4%) of the patients with DSA had poor graft outcome and all had post-TX DSA MFI > 2000. All the pts with pre-TX DSA MFI < 2000 and no DN DSA experienced no graft failure. Pre-tx HLA-DP DSA were detected in 3 out of 10 (30.0%) pts with poor graft outcome, which corroborates recent insights that systematic HLA-DP typing and matching can improve pre-TX risk stratification.

We further described the importance of **prozone effect** for HLA ab data interpretation. In neat serum, complement interference leads to low MFI, while **real prozone** (sera with high MFI but remaining around 20 000 in dilution due to oversaturation of the beads) can occur in EDTA-treated serum (cfr graph). We demonstrate that EDTA treatment abolishes the prozone effect but doesn't overcome the bead saturation effect of high titer abs.
Conclusions: This single center study shows that pre-post TX kinetics of DSA MFI offers a good prognostic marker and risk stratification tool in kidney TX, provided that, at least EDTA-treated serum is used to overcome the prozone effect in LSA.



BOS341 KIDNEY TRANSPLANTATION IN HYPERSENSITIZED PATIENTS WITH AND WITHOUT CIRCULATING PREFORMED DONOR SPECIFIC ANTIBODIES

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Background: Renal transplantation (Tx) in hypersensitized patients (HSP), especially with circulating preformed IgG anti-HLA donor specific antibodies (pDSA) has been associated with increased risk of antibody mediated rejection (AMR) and graft loss.
Materials: We present the results from 56 HSP (%PRA > 70) who received a graft between 2009–2015. The patients (pts) were divided in: group A-37 HSP transplanted without pDSA (MFI < 1000) and group B-19 HSP with pDSA (mean HLA-A-B, -C, -DR, -DQ MFI = 3259 ± 1477, mean HLA-DP MFI = 14 549 ± 13 010). A control group (CG) of 37 non-HSP (%PRA 0–58), transplanted the same period from deceased donors, was also used. All (n = 93) pts were transplanted with negative CDC and T/B FCM. As induction treatment Basiliximab was given to all pts with addition of Rituximab in 15 HS and 2 CG pts. Maintenance immunosuppression of MPA or mTORi/FK506/MP was administered in HSP and of MPA or mTORi/CNI/MP in CG.
Results: During 50 ± 22 follow up months, no significant difference was found between the three groups regarding patients' and donors' age at Tx, AMR episodes, *de novo* DSA, graft loss or infection rates. Biopsy proven acute rejection episodes (n = 9) were developed with no significant difference between the groups: 4/37 group A, 3/19 group B and 2/37CG. The episodes were defined as AMR (n = 3) or T cell mediated rejection (n = 6). All AMR episodes were found in group A (n = 2) and group B (n = 1) pts. The median baseline sCr levels at first month post-Tx was 1.3, 1.2 and 1.4 mg/dl for group A, B and CR respectively (p = NS). Six pts lost the graft: two from group A (one patient with IgM pDSA before Tx and the second from surgical complications), two from group B (surgical complications) and two from CG (chronic rejection with *de novo* DSA in one case). Finally, the current sCr levels (median value) were 1.1, 1.2 and 1.1 mg/dl, with no difference between the A, B, CG groups (p = NS).
Conclusion: We conclude that renal Tx in HSP with and without pDSA and negative CDC and T/B FCM is safe with low immunological risk.

BOS342 FULLY CHIMERIC DNA MATCHING KIDNEY TRANSPLANT WITHOUT IMMUNOSUPPRESSION FOLLOWING BONE MARROW TRANSPLANT

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Background: Over 500 bone marrow transplants (BMT) are followed up at our institution. The BMT is associated with significant morbidity including acute and chronic kidney disease (CKD). CKD is usually secondary to radiation nephropathy and or drug toxicity.
Method and Results: 16 years old patient had history of acute Pre-B lymphoblastic leukaemia that was treated by chemotherapy for 2 years with subsequent development of tubulointerstitial nephritis (TIN), due to chemotherapy and use of aminoglycosides that was proved by kidney biopsy. BMT was done in presence of CKD, and hence his management protocol was modified accordingly.

Two and a half months post BMT, he developed pulmonary finding suggestive of bronchiolitis obliterans with organizing pneumonia (BOOP). This was confirmed by lung biopsy. The BOOP resolved completely with Corticosteroid therapy. Then, he has been on follow up in B.M.T. clinic with gradual withdrawal of immunosuppressant (MMF and steroid) over six months that were stopped all together and was re-immunized for standard communicable disease protocol.

He developed CKD as a result of his original TIN which progressively increased till reached ESKD and started haemodialysis.

Kidney transplant work up was done for him and his sister who was the same donor for BMT. As the patient was fully Chimeric-DNA with his donor, with neither a mismatch nor a history of graft versus host disease, our transplant team decided for only induction with Methylprednisolone 0.5 gm for 2 days followed by oral steroid with gradual tapering over a month. Twice weekly follow up at clinic for one month, he was found vitally stable with stable excellent renal graft function and steroid was stopped and now he is without immunosuppressant.
Conclusion: This was a full chimeric DNA matching kidney transplant that requires no immunosuppression. Both donor and recipient have identical blood groups and tissues types. The clinic follow up showed an excellent graft function.

BOS343 DEVELOPMENT OF SINGLE MOLECULE REAL TIME SEQUENCING OF THE HLA GENOME FOR IMPROVED HIGH-RESOLUTION HLA GENOTYPING

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Background: Currently, organ recipients and donors are genotyped at a low resolution (LR, 1st field) level for HLA–A, B, C, DRB1 and DQB1. In contrast single antigen bead assays allow antibody identification of these loci at a high resolution (HR, 2nd field) level in addition adding other relevant loci such as DQA1, DPA1 and DPB1. This discrepancy between the HLA genotyping and the HLA antibody data compromises the correct assessment of actual donor-recipient match and the risk of donor specific antibodies (DSA) and antibody mediated rejection (AMR). Today HLA labs face the challenge to increase HLA genotyping resolution as well as the number of loci typed for organ transplant recipients and donors.
Materials and Methods: We used the PacBio Single molecule real time sequencing (SMRT) technology with in-house designed primer sets to type 31 samples for Class I HLA-A, B, C at HR resolution level.
Results: The PacBio SMRT sequencing technology allowed us to multiplex 31 samples and genotype them for HLA-A, B and C, resulting in high-quality data without any mistypes compared to the reference data at the HR, 2nd field level. Collaboration with the genomics core in Leuven to process our sample son the PacBio RSII allows us to perform HR HLA genotyping of Class I loci at a cost effective manner which is comparable to that of commercial LR SSO methods, making this approach feasible for implementation in organ transplant recipient, related donor and post-transplant deceased donor allelic resolution genotyping. A similar approach for Class II molecules (DRB1345, DQ, DP) is in development.
Conclusions: New technologies, such as SMRT sequencing (PacBio) allow HLA labs to increase HLA (Class I) genotyping resolution and addresses the current clinical need for high-resolution HLA genotyping in order to comprehend HLA antibody reactivity and the potential risk of DSA and antibody-mediated rejection in organ transplantation.

BOS345 STANDARD LOW-RESOLUTION HLA GENOTYPING OF DONORS IS NOT SUFFICIENT FOR EVALUATING THE RISK OF SEVERE ANTIBODY-MEDIATED KIDNEY ALLOGRAFT REJECTION

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Kidney donor-recipients are matched based on 1st field HLA resolution of a limited number of HLA loci. Techniques to evaluate HLA beyond the 1st field and include other HLA loci in donor typing are available, but their clinical utility has not been established.

A 67 year-old patient with a HLA-*DRB1*03*(DR17) and *DRB1*04*(DR4) genotype, sensitized after her 1st kidney transplant *DRB1*13*(DR13), *DRB1*03* (DR17) showed the direct need to increase resolution and number of HLA target loci studied in deceased donor genotyping. She was offered an apparently well-matched 2nd deceased donor kidney *DRB1*03*(DR17), *DRB1*04*(DR4). Antibody (Ab) identification, had revealed sensitization against the 70DA epitope, shared between DR13 (1st graft) and DRB1*04:02, potentially present in the 2nd donor. As standard low-resolution SSP (Olerup) HLA genotyping doesn't discriminate between the different DR4 2nd field subtypes, an additional high-resolution SSP was performed. The donor was typed DRB1*04:05 allowing TX in the absence of known DSA. Ab-mediated rejection (AMR) was diagnosed on day 5 after TX. The patient also had Abs against 84DEAV, DPB1 (MFI 4000). The donor was genotyped DPB1*01:01, positive for the 84DEAV epitope, identifying this Ab as DSA.

New real time PCR technologies such as the RAPID and SABR kits (Linkage Biosciences) offer the possibility to increase HLA genotyping resolution and loci without the need of additional tests and increased TAT. In a panel of 20 samples, including this case report, we found that the SABR kit clearly distinguishes between common 2nd field HLA alternatives, presenting different HLA epitopes, not only for the currently matched loci HLA-A, -B, -C, DRB1 and DQB1, but also for DRB345, DQA1, DPA1 and DPB1.

We illustrate the need to increase HLA genotyping resolution of donor typing and the feasibility to include other HLA loci, for the correct assessment of DSA at time of TX. The SABR kit meets the criteria to do so.

BOS346 KIDNEY TRANSPLANTATIONS ACROSS IMMUNOLOGIC BARRIERS

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The demand for kidneys continues to exceed the supply. To overcome this problem, efforts to extend the donor pool by including HLA and ABO-incompatible (ABOi) KTs are increasing. The aim of this article was to retrospectively analyze clinical outcomes in ABOi and flow-cytometric cross-match (FCXM) positive KT.

A total of 275 patients who underwent ABOi KT at Asan Medical Center from January 2009 to February 2015 were included in this study. After 42 patients with FCXM positive excluded, 234 patients were divided into Era1 (2009–2012) and Era2 (2012–2015) by desensitization protocol. After we experienced lethal infectious complications, including seven mortalities during Era 1, our center modified the desensitization protocol during Era2. To compare clinical outcomes with ABO-compatible (ABOc) KTs, 600 patients who underwent FCXM negative and ABOc KT from January 2012 to February 2015 were selected as a control group. We also compared clinical outcomes of 45 patients who underwent FCXM positive KT with a control group in the same period.

The overall patient survival (PS) and graft survival (GS) rates stratified by era showed a significant difference between Era1 and Era2 during the 3-year follow-up (PS: 95.5% vs. 100%, $p = 0.009$; GS: 93.9% vs. 98.6%, $p = 0.019$). There, however, was no significant difference between Era2 and control group. The 3-year death-censored GS and rejection free GS among three groups showed no statistical significance. In FCXM positive KT, the overall PS (96.6%), overall GS (96.6%), death-censored GS (100%), and rejection free GS (83.6%) rate at 3 years showed no significant differences with a control group.

ABOi and FCXM positive KT can be performed safely with a successful graft outcome by modification of the immunosuppressive regimen according to the host conditions.

Clinical Kidney Metabolic complications

BOS347 POST-TRANSPLANT SERUM ALBUMIN LEVELS PREDICT BOTH GRAFT FAILURE AND MORTALITY BETTER THAN PRE-TRANSPLANT ALBUMIN LEVELS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The studies concerned the association between serum albumin concentration and post-transplant outcomes in kidney transplant recipients (KTRs) are scarce.
Methods: To evaluate the impact of serum albumin levels on graft and patient survival, we performed a retrospective multi-center cohort study. A total of 2779 KTRs who underwent renal transplantation from Jan 1997 to Jan 2012 were included. Recipients were classified into two groups according to the level of serum albumin (higher albumin group, $\geq$4.0 g/dl vs. lower albumin group, $<$4.0 g/dl).
Results: The mean age of the recipients was 41.7 $\pm$ 11.3 years, and 59.1% were male. When compared with post-transplant albumin levels, the rate of graft failure was higher in lower albumin group compared to higher albumin group in multivariate cox model (Hazard ratio [HR] 1.840, 95% confidence interval [CI] 1.367–2.477, $p < 0.001$), even though eGFR at 1 year after transplantation was not different between the two groups (61.7 $\pm$ 19.8 vs. 62.1 $\pm$ 15.8 ml/min, $p = 0.615$). Both all-cause mortality and non-cardiovascular mortality rates were higher in lower albumin group (HR 2.227, 95% CI 1.258–3.943, $p = 0.006$, and HR 2.784, 95% CI 1.254–6.179, $p = 0.012$, respectively). Every 1.0 g/dL higher serum albumin concentration was associated with 69.2% lower all-cause mortality (HR 0.308, 95% CI 0.196–0.483, $p < 0.001$). However, pre-transplant albumin levels were not associated with both graft failure and mortality. Additionally, post-transplant albumin had higher AUC than pre-transplant albumin in both graft failure (0.605 vs. 0.513) and mortality (0.643 vs. 0.571) in time-dependent ROC curves.
Conclusion: In KTRs, post-transplant serum albumin level is a better prognostic factor for graft failure and mortality than pre-transplant serum albumin level. Therefore, patient with pre-transplant hypoalbuminemia should not be precluded from transplantation. Evaluation and management for hypoalbuminemia should be considered to improve outcomes in KTRs.

BOS348 EFFECT OF NEW ONSET DIABETES AFTER RENAL TRANSPLANTATION ON CARDIOVASCULAR DISEASE AND MORTALITY

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Background: New onset diabetes after renal transplantation (NODAT) is a common problem with high morbidity. It is estimated as one of the factors in the development of cardiovascular disease and mortality. The aim of this study was to evaluate the risk factors of NODAT and its association with development of cardiovascular disease and mortality.
Methods/Materials: All renal transplant recipients that were regularly followed for more than 6 months between January 1998 and August 2006 in Hacettepe University Nephrology Department were included in the study.

Demographic characteristics, pre-transplant dialysis duration, donor characteristics, immunosuppressive drugs, cardiovascular disease history, blood glucose values, hepatitis B, hepatitis C and CMV status, graft failure and mortality information were collected for all subjects.
Results: The study included 708 patients. Median follow-up period was 79 (6–301) months. Median age of the subjects was 41 (18–75) years and 61% of the patients were male. 41 patients had diabetes mellitus before renal transplantation. 109 patients developed NODAT and 558 patients did not developed diabetes after transplantation. Patients with NODAT had higher HCV infection and higher mean age compared to patients that did not developed diabetes after transplantation ($p < 0.001$). Patients with NODAT had 1.76 times (95% CI 0.811–3.851 p: 0.152) and pre-transplant diabetic patients had 3.95 times (95% CI 1.50–10.49 p: 0.05) higher cardiovascular risk compared to non-diabetic patients. Mortality risk was increased 1.73 times (95% CI 0.93–3.22, p: 0.07) in patients with NODAT and increased 3.86 times (95% CI 1.34–11.15 p: 0.01) in pre-transplant diabetic patients.
Conclusion: Advanced age and HCV infections are risk factors for NODAT. NODAT increases the cardiovascular risk and mortality although to a lesser extent compared to pre-transplant diabetic patients.

Clinical Kidney Cardiovascular complications

BOS349 NEW MARKERS IN ASSESSING CARDIOVASCULAR RISK PROFILE IN KIDNEY TRANSPLANT WOMEN

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Background: Despite improvements in patient's and graft's survival, the long-term morbidity and mortality in renal transplant recipients (RTRs) are still high. Beyond traditional cardiovascular (CV) risk factors, the role for new CV risk markers is ascribed to visceral and subcutaneous abdominal depots and liver steatosis. Components of metabolic syndrome are more common among RTRs compared to general population, and it would be expected that these patients have a much higher incidence of non alcoholic fatty liver disease (NAFLD) compared to general population, thus representing a predictor in CV morbidity and mortality.
Materials: 18 RTRs women (median age 40 years, range 19–46), receiving as immunosuppressive therapy (13 pz CyA+MMF+CS, 4 pz CyA+EVE+CS, 1 pz FK+MMF+CS) and basiliximab as induction therapy.
Methods: We investigated NAFLD occurrence and severity, carotid atherosclerosis (intima-media-thickness (IMT) and plaques) by ultrasound. NAFLD was graded by eight-point semi-quantitative severity score, and classified as mild (score < 3), moderate (3–5 score) and severe (≥6 score). Cut-off values for carotid IMT was >0.9 mm, for subcutaneous and visceral adipose thickness >20 mm and >60 mm, respectively. Biohumoral parameters assessing cardiometabolic risk profile were investigated.
Results: Creatinine mean value was 1.41 (±SD 0.77), and CRP mean value was 4.5 (±SD 4.36). As NAFLD is considered, our results showed that 50% of RTRs had moderate/severe, and 28% mild hepatic steatosis; abdominal subcutaneous and visceral lipid depots were not increased. Seven out of 18 (39%) RTRs showed RI >0.70, of whom 57% had also moderate/severe NAFLD. IMT was only increased in one RTR with moderate/severe NAFLD.
Conclusion: Our preliminary data show that RTRs women have a high prevalence of moderate/severe NAFLD not associated with increased abdominal lipid depots. Moreover, in our population NAFLD seems to be not related to vascular damage.

BOS350 THE PREVALENCE AND TREATMENT OF HYPERTENSION IN HEMODIALYSIS PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS IN 2014/2016

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Background: Hypertension is a major problem among the hemodialysis patients (HDp) and kidney transplants recipients (KTRs). It is estimated that it affects more than 80% of those patients. The antihypertensive treatment, especially in this groups often requires a multidrug therapy and individual approach to the patient in order to achieve proper control of blood pressure.
Aim: The aim of the cross-sectional, observational study was to evaluate the prevalence of hypertension, antihypertensive therapy and blood pressure control according to JNC and ESH recommendations in the groups of HDp and KTRs in years 2014/2016.
Material and methods: We studied 86 HDp dialysed in Diaverum Unit and 861 KTRs from Transplantology Outpatients Clinic in 2014/2016 (Table 1).

	KTx (2014)	HD (2016)	p
Amount of participants (*n*)	861	86	<0.05
Man (*n*/%)	515 (59.8)	53 (61.6)	ns
Mean age (years)	52.0	66.2	<0.05
Hypertension (*n*/%)	818 (95.0)	85 (98.8)	ns
Cardiovascular disease (*n*/%)	176 (21.5)	56 (65.9)	<0.05
Diabetes (*n*/%)	190 (23.2)	29 (34.1)	<0.05
Time from KTx (months)	93,8	–	–
Dialysis time (months)	–	45.1	–
Blood pressure < 140/90 (*n*/%)	374 (45.7)	42 (49.4)	ns
4-6 hypertensive drugs (*n*/%)	181 (22.1)	19 (22.3)	ns
3 hypertensive drugs (*n*/%)	238 (29.1)	26 (30.6)	<0.05
2 hypertensive drugs (*n*/%)	222 (27.1)	19 (22.4)	ns
1 hypertensive drug (*n*/%)	147 (18)	12 (14.1)	ns

The analysis of the antihypertensive treatment was based on the medical files and it comprises the comparison of the mean results of blood pressure reported in the six consecutive HD sessions and in the 3 consecutive outpatient visits for HD patients and KTRs, respectively.
Results: The groups in 2014/2016 differed significantly in respect to the prevalence of cardiovascular disease, diabetes and age (Table 1). Hypertension was diagnosed in 95% and 98.8% of HDp and KTRs, respectively.

The target of blood pressure control according to recommendations was reached in 45.7% of KTRs and 49.4% of HDp, respectively ($p > 0.05$). Percentage of patients using single, double, triple and multidrug therapy (4–6) were similar in both groups (Table 1). The most often used drugs were beta-blockers in both groups, followed by calcium channel blockers in KTRs and diuretics in HDp (Table 2).

	KTx (2014)	HD (2016)	p
ß-blockers (n/%)	658 (80.4)	63 (74.1)	<0.05
Diuretics (n/%)	325 (39.7)	59 (69.4)	<0.05
Calcium channel blockers (n/%)	432 (52.8)	45 (52.9)	ns
ACE inhibitors (n/%)	263 (32.2)	17 (20)	<0.05
Sartans (n/%)	54 (6.6)	10 (11.8)	<0.05
α-blockers (n/%)	290 (35.5)	17 (20)	<0.05

Conclusions:

Target of blood pressure control according to recommendations was achieved in less than 50% of patients in both groups.

The pattern of anti-hypertensive therapy differed in the study population.

ß-blockers, diuretics and calcium channel blockers were the most common hypertensive drugs used 2014/2

Clinical Kidney Metabolic complications

BOS351 A SUCCESSFUL APPROACH TO KIDNEY TRANSPLANTATION IN PATIENTS WITH ENTERIC (SECONDARY) HYPEROXALURIA

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Background: Enteric hyperoxaluria due to malabsorption may cause chronic oxalate nephropathy and lead to end-stage renal disease (ESRD). Kidney transplantation is challenging given the risk of recurrent calcium-oxalate deposition and nephrolithiasis.
Patients and Methods: Enteric hyperoxaluria and oxalate deposition can occur both in patients with intact colon and high plasma oxalic acid levels and in patients with ileostomy and relatively low levels. We established a protocol to reduce plasma oxalic acid levels peri-transplantation based on reduced intake and increased removal of oxalate. Cornerstone is low oxalic acid diet (40–50 mg/day), and peri transplantation oxalic acid free drip feed and intensified hemodialysis. We report the outcomes of eight kidney transplantations using this protocol.
Results: Four patients received a living donor kidney and had immediate graft function. Four patients received a deceased donor kidney and had immediate graft function ($n = 1$) or delayed graft function (DGF, $n = 3$). In five patients our protocol was prolonged or re-instituted due to complications in the post-transplantation periods affecting graft function. Complications were: DGF, rejection, sepsis, urinary tract infection, symptomatic native kidney stones, dehydration because of high output stoma. Patients are currently a median of 11 (range 2–28) months after transplantation and all patients have a stable eGFR (49 ± 21 ml/min/1.73 m^2). Oxalate depositions were found in 3 out of the 7 patients who underwent for cause biopsies after transplantation.
Conclusions: This is the first systematic description of kidney transplantation in a cohort of patients with enteric hyperoxaluria. Common complications after kidney transplantation impact long-term transplant function in these patients. With our protocol short-term kidney transplantation outcomes were favorable in this population with unfavorable transplantation prospects and even unsuccessful transplants before.

BOS352 PLASMA LEVELS OF N-6 AND TRANS FATTY ACIDS AND INFLAMMATION EARLY AFTER RENAL TRANSPLANTATION

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Background: Inflammation is a major player after renal transplantation, affecting both short and long-term outcomes. In this cohort, we have previously reported lower levels of pro-inflammatory markers in renal transplant recipients (RTRs) with high levels of marine n-3 polyunsaturated fatty acids (PUFAs) in plasma. Arachidonic acid (AA) and trans fatty acids (TFAs) are considered pro-inflammatory, while the inflammatory properties of linoleic acid (LA) are less known.
Methods/Materials: In a cross-sectional single center study of 850 Norwegian RTRs, transplanted between 2007 and 2011, we assessed associations between levels of TFAs and the n-6 PUFAs LA and AA and levels of pro-inflammatory cytokines soluble tumor necrosis factor receptor 1 (sTNFR1) and interleukin-6 (IL-6) in plasma 10 weeks after transplantation, using multivariate linear regression. Plasma phospholipid fatty acids were determined by gas chromatography. Plasma inflammatory biomarkers were measured by enzyme immunoassays.
Results: A positive association with sTNFR1 was found for AA (Unstd. β-coeff. 1.01, Std. β-coeff. 0.06, $p = 0.02$), whereas neither LA (Std. β-coeff. −0.01, $p = 0.62$) nor TFAs (Std. β-coeff. 0.01, $p = 0.70$) were associated with sTNFR1 levels in plasma. Similar associations were found with IL-6, the downstream product of tumor necrosis factor pathway activation.
Conclusions: No association with inflammatory biomarkers were found for plasma levels of linoleic acid, the major n-6 PUFA. The findings suggest no benefit of linoleic acid consumption shortly before or early after renal transplantation for prevention of inflammation.

BOS353 TRANSPLANTABILITY EVALUATION IN HIGH RISK PATIENTS WITH END STAGE RENAL DISEASE ENROLLED IN THE WAITING LIST OF KIDNEY TRANSPLANTATION. AN OBSERVATIONAL COHORT STUDY

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The outcome of patients with many comorbidities who undergo Kidney transplantation (KTx) in developing countries is not clear. The aim of this study was to find out the risk factors for death on the waiting list (WL) and to determine the time for survival benefit of KTx compared to remaining on dialysis in this high risk patients.

We performed a single-center retrospective analysis of pt's survival on the WL for KTx between Jan/2007 and Dec/2012. Data were obtained from electronic medical records. The follow up (FU) started when pts were enrolled on the WL and it ended on July 31, 2015 when pts were alive or on the date of death when pts died. Statistical analysis were done by Chi-square, cox regression, time dependent cox regression, with $p < 0.05$, CI of 95% and Kaplan Maier, with Log Rank, Breslow and Tarone-Ware post-test.

In 5 years, a total of 1786 patients were included on the WL in our center. The median FU was 3.6 ± 2.3y. In this period, 789 (44.2%) were transplanted, 619 (34.7%) remained on the WL and 378 (21.2%) died. We identified 10 variables that potentially predicted death on the WL. Diabetes Mellitus(DM), arterial coronary disease (CAD), congestive heart failure (CHF), peripheral vascular disease (PVD) and cerebrovascular disease (CVD) were the comorbidities with strongest effect on survival, with adjusted HR varying = 1.8–2.5. The variables that remained significant in the multivariate analyses were age (0.003, HR = 1.03), cause of ESRD ($p = 0.01$, HR = 4.97) and vit D ($p = 0.02$, HR = 0.97).

Pts without comorbidities had a KTx survival benefit after 3 months of FU compared to those who remained on the WL. Pts with PVD and CHF had KTx survival benefit after 6 months of FU; on the other hand, pts with Diabetes, CAD and CVD persisted with high risk of death until the 2nd year. In 3.6 years of FU all patients had better survival after KTx than those remaining on the WL, however patients should be aware of the high initial risk of death compared to staying on dialysis.

BOS354 PREVALENCE AND IMPACT OF POST-TRANSPLANT ANEMIA IN JAPANESE KIDNEY TRANSPLANT RECIPIENTS: THE JAPAN ACADEMIC CONSORTIUM OF KIDNEY TRANSPLANTATION STUDY

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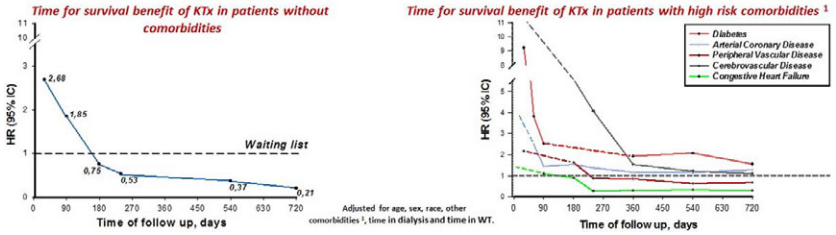
Background: Many kidney transplant recipients (KTRs) still experience various complications during maintenance phase. Post-transplant anemia (PTA) is one of common complication. Nevertheless, this complication has been under-recognized, and not been studied extensively in Japan. Thus PTA has a long and convoluted history of controversy about whether PTA worsens subsequent long-term transplant outcomes.
Methods and Materials: Objectives of this study were to (i) to clarify the change of hemoglobin (Hb) levels and the prevalence within 6 months (mo) after KT; (ii) to determine the magnitude on graft failure; and (iii) to explore which Hb levels at 6 mo has most best sensitivity to predict the subsequent graft loss. We investigated PTA in 1077 adult KTRs between 1995 and 2010. Final follow-up was performed in December 2016 with a median follow-up of 10 years.
Results: The prevalence of PTA was 63% in men and 66% in women at 6 mo after KT according to the WHO definition of PTA. According the WHO criteria, the cumulative 10-year graft failure rates were 17.9% in PTA group and 11.7% in non-PTA group (HR=1.69, 95% CI: 1.15–2.47, $p = 0.007$). We performed sensitivity analysis using ROC curve to clarify optimal cut point of Hb level at 6 mo, and found the threshold of <12 g/dl was more sensitive regardless of gender. According the ROC criteria, the cumulative 10-year rates were 19.7% in PTA group and 12.3% in non-PTA group (HR = 1.78, 95% CI: 1.26–2.50, $p < 0.001$). We next analyzed the 10-year adjusted rates with Cox model after consideration for imbalanced covariates. HRs were 1.50 (95% CI: 1.01–2.22,

Table No. 1

Univariate and multivariate analysis of factors associated with dead in waiting list.

	Univariate analysis		Multivariate analysis	
Variable	*P*	*HR (CI)*	*P*	*HR*
Age, years	0.000	1.05 (1.03 – 1.06)	0.003	1.03 (1.01-1.05)
Educational Stage				
Secondary and tertiary				
Not Schooled	0.002	2.16 (1.32 - 3.53)	0.24	1.72 (0.70 – 4.23)
Primary	0.03	1.30 (1.02 - 1.66)	0.60	1.12 (1.01 – 1.05)
CHF	0.001	1.72 (1.23 - 2.38)	0.72	1.13 (0.59 - 2.17)
Diabetes	0.000	2.12 (1.69 - 2.64)	0.19	0.58 (0.26 – 1.32)
PVD	0.000	2.55 (1.87 - 3.48)	0.59	1.22 (0.60 – 2.49)
CAD	0.000	1.87 (1.47 - 2.37)	025	0.71 (0.39 - 1.28)
CVD	0.003	1.82 (1.23 - 2.70)	0.89	0.95 (0.44 - 2.02)
Smoking				
Non smoker				
Current smoker	0.32	1.18 (0.85 - 1.64)	0.92	1.03 (0.54 – 1.96)
Past smoker	0.03	1.32 (1.03 - 1.69)	0.75	0.90 (0.48 – 1.68)
Serum Vitamin D, ng/ml	0.02	0.98 (0.97 - 0.97)	0.02	0.97 (0.95 - 0.99)
Cause of ESRD				
PKD				
Hypertension	0.18	1.54 (0.82 - 2.89)	0.33	1.71 (0.58 – 4.99)
Glomerulonephritis	0.81	0.92 (0.48 - 1.78)	0.49	1.48 (0.48 – 4.61)
Diabetes	0.006	2.23 (1.26 - 4.12)	0.01	4.97 (1.44 – 17.23)
Others	0.99	1.00 (0.49 - 2.02)	0.71	2.78 (0.92 – 8.45)

PVD: Peripheral Vascular Disease, CHF: Congestive heart failure, CAD: Arterial coronary disease, CVD: Cerebrovascular disease, ESRD: end-stage renal disease,



p = 0.043) and 2.04 (95% CI: 1.42–2.92, p < 0.01) using the WHO and ROC criteria, respectively.
Conclusions: High PTA occurred at 6 mo maintenance period, and PTA was associated with an increased risk of graft failure. However, our results suggest the WHO criteria potential to have less sensitivity for predicting subsequent graft failure in Japanese KTRs.

Clinical Kidney Cardiovascular complications

BOS355 THE IMPACT OF CHANGES IN BODY MASS INDEX ON CARDIOVASCULAR OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: A higher body mass index (BMI) before kidney transplantation (KT) is associated with increased mortality and allograft loss in kidney transplant recipients (KTRs). However, the impact of changes in BMI after KT on these outcomes remains uncertain. The aim of this study was to investigate the effect of baseline BMI and changes in BMI on clinical outcomes in KTRs.
Methods: A total of 869 KTRs were enrolled from a multicenter, observational cohort study between 2012 and 2015. Patients were divided into low and high BMI groups before KT based on a BMI cut-off point of 23 kg/m^2. Differences in acute rejection and cardiovascular disease (CVD) between the two groups were analyzed. In addition, clinical outcomes across the four BMI groups divided by BMI change 1 year after KT were compared. Associations between BMI change and laboratory findings were also evaluated.
Results: Patients with a higher BMI before KT showed significantly increased CVD after KT (p = 0.027) compared to patients with a lower BMI. However, among the KTRs with a higher baseline BMI, only persistently higher BMI in KTRs was associated with increased CVD during the follow-up period (p = 0.003). Patients with persistently higher BMI had significantly decreased high-density lipoprotein cholesterol and increased hemoglobin, triglyceride, and hemoglobin A1c levels. Baseline BMI and post-transplant change in BMI were not related to acute rejection in KTRs.
Conclusions: BMI in the first year after KT as well as baseline BMI were associated with CVD in KTRs. More careful monitoring of obese KTRs who do not undergo a reduction in BMI after KT is required.

Clinical Kidney Metabolic complications

BOS356 PRE- AND POST-TRANSPLANT SERUM ALKALINE PHOSPHATASE PREDICTS GRAFT FAILURE AND MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Recent studies showed that high levels of serum alkaline phosphatase (AlkPhos) are associated with all-cause or cardiovascular death in chronic kidney diseases. However, there are apparently no data on the effect of AlkPhos in kidney transplant recipients (KTRs). The aim of this study was to evaluate whether serum AlkPhos is associated with graft failure and mortality after kidney transplantation.
Methods: Among the 3029 kidney transplant recipients (KTRs) who were enrolled in a multicenter cohort, we examined the association of pre-transplant serum AlkPhos levels and long-term outcomes in KTRs.
Results: Pre-transplant serum AlkPhos ≥ 80 IU/l was associated with a hazard ratio (HR) for graft failure of 1.571 (95% CI 1.146–2.152, p = 0.005) in a fully adjusted model. Death censored graft failure (DCGF) rate in kidney recipients gradually increased along the increments of AlkPhos. Also, a rise in serum AlkPhos by 40 IU/l during the first 3 months after kidney transplantation was associated with higher rates of DCGF (HR 2.353, 95% CI 1.506–3.676) and higher rates of mortality (HR: 2.733, 95% CI 1.479–5.050). Cox regression models using time-varying AlkPhos demonstrated significant relationships between AlkPhos and DCGF (HR 1.39, 95% CI 1.04–1.84) or mortality (HR 2.14, 95% CI 1.39–3.27).
Conclusion: Increased pre- and post-transplant serum AlkPhos and a rise of serum AlkPhos during early period after kidney transplantation is associated with graft failure and mortality in kidney transplant recipients.

BOS357 ESTIMATED GLOMERULAR FILTRATION RATE IS NOT RELIABLE IN KIDNEY TRANSPLANT RECIPIENTS WITH ADVANCED GRAFT FAILURE

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Background: The equations for glomerular filtration rate (GFR) estimation are not always reliable in specific populations such as kidney transplant recipients. The purpose of our study was to determine the performance of GFR equations in patients with advanced failure of the transplanted kidney.
Methods: This prospective clinical study included 13 adult patients (5 men, 8 women) with kidney graft in pre-dialysis stage (GFR < 15 ml/min/1.73 m^2). Estimated GFR with Modification of Diet in Renal Disease equation (MDRD), Chronic Kidney Disease Epidemiology Collaboration equation (CKD EPI) with serum creatinine concentration (CKD EPI Cr), serum cystatin C concentration (CKD EPI CysC) or both (CKD EPI Cr-CysC) and creatinine clearance calculated with Cockcroft-Gault equation (CG) was compared with measured GFR with ^{51}Cr-EDTA clearance (mGFR ^{51}Cr-EDTA). Body composition was measured with bioimpedance analysis.
Results: The mean value of mGFR ^{51}Cr-EDTA was 9.6 ± 3.1 (from 5.7 to 14.9) ml/min/1.73 m^2. All of the estimating equations overestimated the mGFR ^{51}Cr-EDTA by a significant degree ($p < 0.05$) shown as bias (the difference between estimated GFR and mGFR ^{51}Cr-EDTA) ± SD (estimation of precision) in ml/min/1.73 m^2 with 30% accuracy in brackets (measured as the percentage of results that did not deviate more than 30% from the mGFR ^{51}Cr-EDTA): CG 17.4 ± 12.3 (0%), MDRD 15.1 ± 16.3 (8%), CKD EPI Cr 15.6 ± 17.3 (8%), CKD EPI CysC 11.1 ± 7.5 (15%), CKD EPI Cr-CysC 11.8 ± 9.7 (15%). Analysis of body composition showed that 10 patients (77%) had reduced proportion, 2 (15%) had normal proportion and only 1 (8%) had increased proportion of lean body mass (body mass without lipid component), as we would expect for their age and sex.
Conclusion: The most often used GFR estimating equations were not reliably accurate or precise in our patients with advanced renal graft failure. Modified body composition with lower proportion of lean body mass could be the most likely reason for such results.

Clinical Kidney Cardiovascular complications

BOS358 ASSOCIATION BETWEEN MATRIX-GLA PROTEIN AND AORTIC STIFFNESS IN KIDNEY TRANSPLANTATION

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Background: Aortic stiffness due to vascular calcifications is commonly observed among renal transplant recipients (RTR) and is considered as a predictive factor of poor events such as cardiovascular (CV) events and graft failure. Matrix-gla protein (MGP) is an inhibitor of vascular calcifications. In kidney transplantation, a recent study has shown a significant association between the inactive form of MGP (dephosphorylated and uncarboxylated MGP, dp-ucMGP) and all-cause mortality and transplant failure. However, no data showing an association between dp-ucMGP and the risk of vascular calcifications is yet available. The aim of our study was to assess the association between MGP and aortic stiffness in a cohort of RTR.
Materials/Methods: We studied the association between the circulating levels of dp-ucMGP, vascular calcifications (Kauppila score) and aortic stiffness (oscillometric method and applanation tonometry) in prevalent RTR. The association was assessed by performing uni- and multivariate analysis including parameters such as traditional and nontraditional CV risk factors, pulse wave velocity (PWV) and estimated GFR (MDRD).
Results: We analyzed 128 patients in two independent centers. The mean age of this cohort was 55.4 ± 13.6 years and the mean time since transplantation was 8.3 ± 7.7 years. In univariate analysis, a significant association was observed between MGP and PWV. In multivariate analysis, we showed that the factors independently associated with PWV were age, diabetes mellitus, eGFR and MGP. No association was found between MGP and the Kauppila score.
Conclusion: Our data suggest the existence of a significant and independent association between MGP levels and elevated aortic stiffness in RTR. The absence of correlation between MGP and vascular calcifications may be explained by the lack of sensibility of the Kauppila score Theses results need to be confirmed among a largest and prospective study to assess the role of MGP as a marker of CV risk in RTR.

BOS359 TEMPORAL VARIATIONS IN THE IMPACT OF COMORBIDITY ON SURVIVAL AFTER RENAL TRANSPLANTATION

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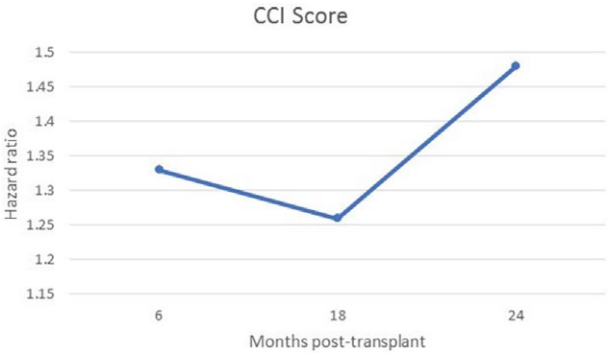
Introduction: Comorbidity is increasingly common amongst renal transplant recipients, yet its impact on outcomes is not well described. We investigated the impact of comorbidity on survival after renal transplantation and whether this changes over time.
Methods: 2262 adult renal transplant recipients were recruited from all 23 UK renal transplant centres between 2011–13 as part of the ATTOM study. Comorbidity data were collected at the time of transplantation. Overall survival at 24 months was analysed using Kaplan-Meier estimates. The impact of a comorbidity score (modified Charlson index) on patient survival was analysed for the time periods 0–6 months, 6–18 months and 18–24 months post-transplantation using Cox proportional hazards regression models. Each time period was modelled separately, considering only those at risk within that period (i.e. excluding those who did not survive to the next time period).
Results: Overall patient survival at 24 months post-transplantation was 96.5% (confidence interval CI, 95.6–97.2%). The higher the comorbidity score, the poorer the survival at 24 months ($p < 0.0001$). The impact of comorbidity on patient survival was modelled for the 3 time periods separately, and adjusted for patient age, donor age and living or deceased donor. Between 0–6 months, a 1 point increase in comorbidity score was associated with a hazard ratio (HR) of 1.33 (CI 1.10–1.60, $p = 0.003$), between 6–18 months the HR decreased to 1.26 (CI 1.03–1.55, $p = 0.027$) and between 18–24 months the HR increased to 1.48 (CI 1.24–1.77, $p < 0.0001$). This demonstrates that the impact comorbidity score on patient survival followed a J-shaped curve over time (Figure 1).

Conclusions: Higher comorbidity is associated with poorer patient survival post-transplantation. The impact of comorbidity changes over time and these variations should be accounted for in any survival benefit models.



BOS360 INFLUENCE OF GENE POLYMORPHISMS ON SERUM FETUIN-A LEVELS AND VASCULAR CALCIFICATIONS IN RENAL TRANSPLANT AND CHRONIC KIDNEY DISEASE PATIENTS

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Serum fetuin-A is a major systemic inhibitor of vascular calcifications. Aim of this study was to determine frequency of single nucleotide polymorphisms in gene for fetuin-A: Thr248Met C>T (rs4917) i Thr256Ser C>G (rs4918), their association with serum fetuin-A levels and coronary artery calcifications (CAC) in renal transplant (RT) and chronic kidney disease (CKD) patients.

We evaluated 97 patients, 49 RT patients (GFR 39.60 ± 15.04 ml/min/1.73 m^2) and 48 patients with CKD level 2–5 (GFR 30.86 ± 22.17 ml/min/1.73 m^2) regularly monitored at Clinic for nephrology CCS during 72 months. Serum creatinine, high sensitive C reactive protein (hs-CRP), interleukin-6, serum amyloid A, as well as fetuin-A (ELISA Epitope Diagnostics, Inc., San Diego, California, USA) concentration were determined. CAC score was evaluated using multi-detector row spiral computed tomography (MSCT).

Detection and analysis of single nucleotide polymorphisms were performed using PCR method.

Frequency of mutations in rs 4917 gene was 34%. Genotype CC had 43 (44.3%) patients, 41 (42.3%) were heterozygotes CT and 13 (13.4%) were homozygotes with mutant allele TT. Complete linkage disequilibrium between rs4917 and rs4918 was found and in further analysis only data for rs4917 polymorphism were reported. Presence of TT genotype correlated with lower fetuin-A levels (0.375 ± 0.11 g/l) in comparison to CC genotype (0.469 ± 0.11 g/l, $p = 0.019$). Median of fetuin-A levels was 0.437 g/l. Patients with fetuin-A levels below median had CAC more frequently (51.2% vs. 24.4%, $p = 0.01$) and higher parameters of inflammation (fibrinogen 5.09 vs. 4.43 g/l, $p = 0.022$, hsCRP 1.19 vs. 0.44 mg/l, $p = 0.046$) in comparison to patients with fetuin-A levels above median. Logistic univariate analysis indicated age ($p = 0.000$), fetuin-A ($p = 0.011$) and rs 4917 polymorphism ($p = 0.021$) as predictors of CAC.

Polymorphisms in rs 4917 and rs 4918 genes were associated with lower fetuin-A levels and increased risk for CAC in RT and CKD patients.

Translational Kidney Biomarkers and molecular changes

BOS361 MONITORING IMMUNOSUPPRESSIVE DRUG EFFECTS IN T CELL SUBSETS BY PHOSPHO-SPECIFIC FLOW CYTOMETRY

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Pharmacokinetic drug monitoring, based on pre-dose concentrations, shows a poor correlation with the occurrence of acute rejection after transplantation. A superior method for biological monitoring of tacrolimus (TAC) and belatacept (BELA) in T cell subsets of transplant patients might be phospho-specific flow cytometry of stress-related signaling molecules, downstream of T cell activation pathways.

Blood samples from kidney transplant patients were monitored pre and during the first year after transplantation. Patients received maintenance therapy consisting of TAC ($n = 20$) or BELA ($n = 20$) in combination with mycophenolate mofetil, prednisolone and basiliximab induction therapy. p38MAPK, ERK and Akt phosphorylation (MFI) in T cell subsets was measured by phospho-specific flow cytometry after PMA/ionomycin stimulation. Isotype controls were used as negative controls.

After transplantation, in unstimulated samples, p-p38MAPK and p-Akt were inhibited in $CD8^+$ cells (respectively 5% and 6% mean inhibition; $p < 0.05$) and p-ERK in $CD4^+$ cells (11%; $p < 0.05$) only in a TAC-based therapy.

The effect of immunosuppression on phosphorylation of these signaling molecules was also measured in activated T cells. For that end, blood samples were polyclonal activated and compared to pre-transplantation. After transplantation, the expression of p-p38MAPK and p-AKT were significantly inhibited in $CD8^+$ cells (24% and 15%, respectively; $p < 0.05$) and $CD4^+$ cells (24% and 17%; $p < 0.05$) when TAC was given and not in BELA treated patients. BELA only inhibited p-ERK in $CD4^+$ cells (18%; $p < 0.05$).

Eleven out of 20 BELA-treated patients had a biopsy proven acute rejection, which was associated with higher p-ERK levels in $CD4^+$ and $CD8^+$T cells compared to patients without a rejection ($p < 0.05$).

Phospho-specific flow cytometry is a novel tool to monitor pharmacodynamic effects of TAC. BELA-based immunosuppression does not inhibit key T cell activation pathways which may contribute to the high rejection incidence in BELA-treated patients.

Basic Liver Biomarkers and molecular changes

BOS362 BILE DUCT STRICTURES AFTER LIVER TRANSPLANTATION ARE ASSOCIATED WITH A DONOR GLYPICAN-6 POLYMORPHISM LINKED TO THE BILIARY STEM CELL NICHE

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Background : Both anastomotic strictures (AS) and non-anastomotic strictures (NAS) are two of the most common complications after liver transplantation. The origin seems multifactorial but damage to bile duct stem cell niche is found to play an important role. The proteoglycan Glypican-6 (GPC-6) has been identified as an important cell surface factor for stimulating Wnt-receptor signaling in epithelial stem cells (Fig 1A). GPC-6 gene polymorphisms are associated with bile duct disease in PSC patients, but the role of GPC-6 in bile duct strictures post transplantation has not been established

Methods : Human extra-hepatic bile ducts were collected to culture biliary stem cells which self-organize in to bile duct organoids (Fig 1B). Biliary stem cells, differentiated cholangiocytes and CCA cell lines were analyzed for mRNA GPC-6 expression by qPCR. Single nucleotide polymorphism (SNP) of GPC-6 was analyzed in a retrospective cohort of liver donors and recipients.
Results : In organoid cultures of bile duct stem cells, GPC-6 mRNA was clearly detectable and expression was reduced after differentiation toward mature cholangiocytes. Also two cholangiocarcinoma cell lines had low GPC-6 expression. The GPC-6 SNP could be identified in 309 recipients, 241 donors and 201 paired donor-recipient combinations. Of the recipients without PSC, biliary strictures occurred in 37%. Distribution of the GPC-6 SNP was similar in recipient and donor ($p = 0.818$). Donor GPC-6 AA genotype was associated with the development of biliary strictures (Fig 1C $p = 0.021$). Multivariate analysis with other known risk factors showed GPC-6 AA genotype as an independent risk factor for biliary strictures (HR 2.34 $p = 0.050$).
Conclusions : Donor GPC-6 AA genotype is an independent risk factor for the development of bile duct strictures after liver transplantation in non-PSC recipients. The exact relationship of GPC-6 and bile duct injury may be based on decreased Wnt-activation of bile duct stem cells in the peribiliary glands.

Translational Kidney Biomarkers and molecular changes

BOS363 MICRORNAS IN URINE HELP TO IDENTIFY ACUTE REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: MicroRNAs (miRs) are small non-coding RNAs, with high stability in body fluids. The aim was to determine the predictive value of a combined cellular/molecular biomarker platform in urine for the non-invasive detection of acute rejection after kidney transplantation.
Methods/Materials: In a retrospective cross-sectional study, miR expression profiling (Exiqon qPCR panels) was performed on transplant biopsies ($n = 7$) and urine sediments ($n = 8$) of renal transplant recipients with a biopsy proven acute rejection. Eight biopsies and urine sediments from recipients with a stable graft function represented the control group. The expression of 15 miRs of interest was quantified with qPCR in an independent set of 115 urine sediments of patients with biopsy-supported acute rejection and 55 urine sediments from patients without histological signs of acute rejection in a protocol biopsy. Paired urine supernatant was assessed for protein levels of CXCL-9, CXCL-10, S100A8/A9 heterodimer, and soluble HLA class I.
RESULTS: Five of the fifteen candidate miRs were differentially expressed in urine between the rejection and control group, including miR-155-5p (6-fold), miR-126-3p (4.5-fold), miR-21-5p (3.1-fold), miR-25-3p (2.4-fold), and miR-615-3p (0.4-fold). CXCL-9 and CXCL-10 protein levels were significantly elevated (>8-fold) in urine supernatant from recipients with acute rejection. There was no significant difference for any analyte between samples from recipients with T-cell mediated rejection and those with antibody-mediated rejection. In a multivariate model, miR-155p, miR-25-3p, miR-615-3p, along with CXCL-9 levels, donor type, and recipient age were independent predictors of acute rejection (sensitivity 94.6%, specificity 87.8%).
Conclusion: A combined measurement of miR expression in urine sediment and chemokines in urine supernatant from renal transplant recipients helps to non-invasively identify acute transplant rejection.

BOS364 CO-INHIBITORY PROFILE AND CYTOTOXICITY OF CD57+ PD-1- T-CELLS IN BELATACEPT TREATED KIDNEY TRANSPLANT RECIPIENTS

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Background: Belatacept (BELA)-based therapy after kidney transplantation is associated with an increased risk of rejection compared to ciclosporin-based therapy. Since BELA inhibits the CD28-CD80/86 pathway, CD28- T-cells, expressing high amounts of CD57, are not susceptible to this treatment. High expression of CD57 is the result of chronic antigenic stimulation. Numbers of pre-transplant CD4 + CD57 + PD1- T-cells have been identified as a new biomarker predicting BELA-resistant rejection, although conflicting data have been reported. The aim of this study was to assess the alloreactive potential of CD4 + CD57 + PD1- T-cells and inhibitory properties of BELA.
Methods: We studied co-inhibitory signals as markers for senescence (CD223, CD244 and PD1), proliferative capacity (Ki67) and cytotoxic capacity (granzyme B) of pure FACS-sorted CD4 + CD57 + PD1- T-cells after donor antigen stimulation, and used CD4 + CD57-PD1- T-cells as controls. Also, the effect of BELA on the cytotoxic capacity was tested in donor-antigen stimulated

peripheral blood mononuclear cells from 19 patients pre-transplantation, who received BELA-based therapy after transplantation.
Results: Expression of CD223 increased by 10% after donor antigen stimulation in all 4 T-cell subsets. Proliferation and upregulation of CD244 and PD1 was observed on CD4 + CD57-PD1- T-cells after donor antigen stimulation, but no upregulation of these markers occurred on CD4 + CD57 + PD1- T-cells. However, granzyme B expression was upregulated in CD4 + CD57 + PD1- T-cells. BELA only marginally inhibited granzyme B expression in donor-antigen activated CD4 + CD57 + PD1- cells (median inhibition 31%, $p < 0.01$). Inhibition of granzyme B expression was comparable in all T-cell subsets studied between patients with or without an acute rejection episode.
Conclusion: CD4 + CD57 + PD1- T-cells showed a senescent but more cytotoxic profile than their CD57- counterparts. Their cytotoxic capacity can be partly inhibited by BELA and was not associated with rejection development.

Clinical Kidney Biomarkers and molecular changes

BOS365 URINARY METABOLIC PROFILES TO PREDICT PROLONGED DURATION OF DELAYED FUNCTION IN DCD KIDNEY TRANSPLANT RECIPIENT

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Background: Extending donor criteria, including donation after circulatory death (DCD) kidney donors, has resulted in increased rates of delayed graft function (DGF). Understanding the mechanisms of DGF is crucial for monitoring the natural recovery from DGF. In the current study in DCD recipients, we analyzed urinary metabolic profiles, measured by Nuclear Magnetic Resonance (NMR) spectroscopy, in relation to the presence and duration of functionally defined DGF (fDGF).
Methods: A total of 92 consecutive DCD recipients were included. All patients received anti-CD25 antibody induction and triple maintenance therapy (CNI, steroids, MMF). Day 10 urine samples were analyzed with NMR and the concentrations of 48 metabolites were quantified and evaluated with univariate statistical methods.
Results: In patients with fDGF, 8 metabolites were significantly increased and 6 metabolites significantly decreased as compared to patients without fDGF. In patients with prolonged fDGF (≥21 days) only 2 metabolites were significantly different as compared to patients with fDGF <21 days; lactate increased (mean difference = 0.60, $p = 0.044$), while pyroglutamate decreased (mean difference = −0.75, $p = 0.044$). In order to improve predictability of prolonged fDGF a set of metabolite ratios were calculated and an optimal subset of the ratios was selected. A logistic regression model, built using this optimal set of the ratios (leucine/fumarate, lactate/succinate, betaine/pyroglutamate and leucine/creatinine), adequately predicted prolonged fDGF with an AUC of 0.87.
Conclusion: Kidney transplant recipients with fDGF can be identified with an altered urinary metabolome. The metabolites associated with prolonged fDGF are all handled by proximal tubular epithelial cells and therefore most likely reflects tubular function. Our results show that NMR spectroscopy could be a robust analytical tool to adequately predict prolonged fDGF.

Translational Kidney Biomarkers and molecular changes

BOS366 MICRORNA-21 (MIR-21) IS A USEFUL BIOMARKER OF KIDNEY INJURY AND MAYBE ABLE TO PREDICT OUTCOMES PRIOR TO TRANSPLANTATION

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Introduction: Ischaemia Reperfusion Injury (IRI) is an inevitable consequence of transplantation that leads to delayed graft function (DGF). MicroRNAs, important post-transcriptional regulators of gene expression, have considerable potential as biomarkers in numerous disease processes, including kidney disease. Of particular interest, increased expression of miR-21 has been reported in acute kidney injury (AKI). We have also recently shown an association between miR-21 expression in hypothermic machine perfusate (HMP) samples (from kidneys perfused on the Lifeport®) and post-transplant graft function. The aims of this research were to determine whether miR-21 was a useful marker of kidney injury in other settings by determining its expression in *in vivo* model of IRI and in urine samples from kidney transplant patients with DGF.
Methods: An *in vivo* model of IRI was utilised, in which adult male lewis rats underwent left unilateral 45 min IRI ($n = 5$) and sham operation ($n = 5$). Kidney tissue was retrieved at 48 h. Histological, mRNA AKI marker (NGAL and KIM-1) and miR-21 analyses were undertaken.
First-pass urine samples were collected from kidney transplant patients with and without DGF ($n = 33$) for RNA extraction and miR-21 measurement.
Results: IRI was characterised by marked histological damage (including acute tubular necrosis and endothelial cell loss) and increased mRNA expression of NGAL and KIM-1. MiR-21 expression was significantly up-regulated by 2.5-fold in IRI versus sham.
Expression of miR-21 within urine samples from kidney transplant patients with DGF was significantly up-regulated by 20-fold compared to patients without DGF.
Conclusions: These data show that miR-21 expression is a useful marker of kidney injury in the context of transplantation. Moreover, it shows huge potential in being able to predict early outcomes from kidney transplantation. Further studies are needed with larger patient cohorts to confirm these findings.

Basic Kidney Biomarkers and molecular changes

BOS367 PROTEOMIC CHANGES IN LIVING KIDNEY DONORS IN RESPONSE TO LAPAROSCOPIC DONOR NEPHRECTOMY AND PROPOFOL OR SEVOFLURANE ANAESTHESIA

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Background: Surgical trauma induces perioperative stress impacting on systemic inflammatory and humoral responses that are associated with more or less postoperative comorbidity. Different types of anaesthesia are known to selectively depress normal physiological processes including T-cell and B-cell responses. In this study the biological effect of the surgical intervention combined with propofol or sevoflurane anaesthesia in living kidney donors undergoing laparoscopic surgery was assessed by proteome profiling of blood plasma samples.
Materials/methods: Longitudinal plasma samples were obtained before surgery (T0), immediately after surgery (T1), and 24 hours after surgery (T2) from patients anaesthetised with either propofol ($n = 19$) or sevoflurane ($n = 17$) and matched by age, gender, and BMI. Samples were subjected to proteome profiling by mass spectrometry followed by data analysis with MaxQuant software and relevant statistical methods.
Results: Quantitative protein identification resulted in detection of 633 plasma proteins. A subset of 28 proteins showed statistically significant ($p < 0.05$) expression level changes between time points. Proteins with over two-fold change comprised a smaller group of 9 upregulated targets that are known to be involved in acute phase inflammatory response (CRP, SAA1, SAA2, LBP, SERPINA1, SERPINA3) and tissue regeneration (FGL1, LRG1, MAN1A1). These targets were common in all patients, except MAN1A1 that was upregulated only in propofol anaesthesia.
Conclusion: The highest detected changes in protein levels were found to be independent of anaesthesia type, while proteome profiles also displayed a number of moderate level anaesthesia-specific changes. More proteins with statistically significant level changes were detected one day after surgery (T2) as compared to immediately after surgery (T1), in both anaesthesia groups. Affected proteins involved in a delicate balance between acute phase inflammatory and tissue regenerative process.

Translational Kidney Biomarkers and molecular changes

BOS368 FP7 BIOMARGIN: SMALL SETS OF URINARY CELL MRNAS LEADING TO A PARTITION TREE ON KIDNEY ALLOGRAFT LESIONS

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Background: FP7 Biomargin aimed at detecting and validating non-invasive biomarkers of kidney graft lesions. In this study, we investigated the diagnostic

potential of messenger RNAs (mRNAs) in urine samples. After screening of candidate biomarkers in a case-control study, their diagnostic performance was evaluated in a larger trans-sectional study.
Methods/Materials: Urine samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Patients were retrospectively selected after centralized histological reading of their biopsy by expert pathologists, and classified into 4 groups (normal, ABMR, TCMR or IF/TA). Absolute quantification of mRNAs was performed on urine cell pellets by qPCR. A statistical pipeline was applied to identify which biomarker candidates were associated with one of the 4 groups. Multivariate models were built to define parsimonious subsets of mRNAs that collectively were highly associated with graft lesions.
Results: A total of 24 mRNAs was quantified on 238 urine cell pellets from the case-control study, which included 73 Normal, 34 TCMR, 71 IF/TA and 60 ABMR samples. A set of 4 mRNAs differentiates patients with a biopsy showing acute rejection (AMBR or TCMR) from a normal biopsy (mean AUC = 0.73). Another set of 3 mRNAs discriminates the patients with a biopsy showing acute rejection from IFTA (mean AUC = 0.72). Finally, among the rejection group, a 4 gene signature enables to distinguish ABMR from TCMR (mean AUC = 0.77).
Conclusion: We identified small subsets of urine mRNAs, which enable a multistep approach to discriminate patients into 4 clinically relevant situations. These non-invasive molecular signatures could advise clinicians on the indication of performing a biopsy. The diagnostic performance of our mRNA signatures is currently been investigated in a trans-sectional set of urine samples, obtained at the time of 458 biopsies. Their predictive performance will then be assessed in a prospective study.

BOS369 DYNAMICS OF CD25-POSITIVE MYELOID SUPPRESSOR CELLS IN SOLID ORGAN TRANSPLANTED PATIENTS AND RELATIONSHIP WITH REJECTION

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Background: Myeloid derived suppressor cells (MDSC) are immature cells with immunosuppressive capacities. Three MDSC subsets are currently defined: M-MDSC, eMDSC and PMN-MDSC. MDSC increase in cancer and chronic infections and associate with poor prognosis, but their role in transplantation (Tx) is unknown. Changes in MDSC could provide biomarkers of graft evolution, and they could be useful as immunosuppressive therapy and to stimulate the allograft tolerance.
Methods: Peripheral blood MDSC were identified in cohorts of kidney ($n = 164$) and liver ($n = 30$) recipients and healthy volunteers (HV) as CD33 + CD11b+HLA-DRlo/-. We characterized CD14 + CD15− (M-MDSC) and CD14-CD15- (eMDSC) subsets. Suppression assays and measurement of surface CD25 expression (MFI) on MDSC were performed.
Results: Renal recipients MDSC were able to suppress T cell proliferation *in vitro*. MDSC % were similar in pre-transplant, kidney transplant recipients (KTR), than in HV. MDSC and M-MDSC increased, mainly at 7 and 14 days post-Tx (3.48% and 3.85% vs. 1.14%; 2.47% and 2.48% vs. 0.24% $p \leq 0.001$ vs. pre-Tx).

The increase of MDSC in KTR with basiliximab as induction therapy was lower than in patients induced with thymoglobulin or without induction, and eMDSC were particularly decreased in basiliximab-treated patients (vs. no induction, $p \leq 0.05$; vs. thymoglobulin, $p \leq 0.05$). We confirmed that eMDSC expressed CD25, target of basiliximab. Pre-Tx, liver transplant recipients (LTR) had higher % of CD25 + eMDSC and higher CD25 MFI than KTR and HV. In LTR and KTR without basiliximab, % and MFI of CD25 in eMDSC increased after transplant. In KTR cohort, 7% of patients suffered acute rejection (AR). Absolute numbers of MDSC at 7 days post-transplant (measured before the rejection event) were significantly lower in AR than in non-rejectors (25.84 cells/μl vs. 53.18 cells/μl respectively, $p \leq 0.05$).
Conclusions: M-MDSC increase post-Tx. Low MDSC counts significantly preceded rejection. eMDSC express CD25 which upregulates after Tx.

BOS370 A COMPOSITE SCORE ASSOCIATED WITH SPONTANEOUS OPERATIONAL TOLERANCE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: New challenges in renal transplantation include using biological information to devise a useful clinical test for discerning high- and low-risk patients for individual therapy and ascertaining the best combination and appropriate dosages of drugs.
Methods: Based on a 20-genes signature from a microarray meta-analysis, with 46 operationally tolerant patients and 266 renal transplanted recipients with stable function, we applied the sparse Bolasso methodology to identify a minimal and robust combination of six genes and two demographic parameters as significantly associated with operational tolerance.
Results: This composite score of operational tolerance (cSoT) discriminates operationally tolerant patients with an AUC of 0.97 (95% CI = 0.94–1.00). The cSoT is not influenced by immunosuppressive treatment, center of origin, donor type, or post-transplant lymphoproliferative disorder history of patients. The cSoT is associated with *de novo* anti-HLA antibodies ($p = 0.0011$) and tolerance loss ($p = 0.026$). This score was validated by quantitative PCR (AUC = 0.84, 95% CI = 0.65–1.00) and demonstrated specificity toward a model of tolerance induction. We also measured this score in urine samples.
Conclusion: With 6 genes and 2 demographic parameters, this simple score would provide inexpensive risk stratification for individual immune tolerance status of recipients and may improve follow-up of patients, thus paving the way for individual therapy.

Clinical Liver Biomarkers and molecular changes

BOS371 THE COMBINATION OF DES-GAMMA CARBOXY-PROTHROMBIN AND ALPHA-FETOPROTEIN IMPROVES THE ABILITY TO PREDICT RECURRENCE OF HEPATOCELLULAR CANCER AFTER LIVER TRANSPLANTATION IN A EUROPEAN SETTING

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The role of des-gamma carboxy-prothrombin (DCP) in the prediction of hepatocellular cancer (HCC) recurrence after both hepatic resection (HR) and liver transplant (LT) has almost only been investigated in the Eastern world. Studies in the West are very scarce as are those addressing the value of the combination of DCP and alpha-fetoprotein (AFP) as prognosticators of tumor aggressiveness and recurrence. Recently, the Korean SNUH group has proposed a new (MoRAL) score in relation to HCC recurrence after LT based on such combination. The present study aims at investigating in a European setting HCC aggressiveness based on the evaluation of hepatic, inflammatory and both AFP/DCP tumor markers.

One hundred seventy-one HCC patients underwent LT ($n = 141$) or HR ($n = 30$) during the period July 2010-January 2017 in two collaborative European centres (UCL-Brussels, Belgium [$n = 126$] and Ancona, Italy [$n = 45$]).

Six different markers were investigated as possible predictors of six well-known pathological tumor conditions typically connected with a higher risk for recurrence: model for end-stage liver disease (MELD), neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte ratios (PLR), AFP, DCP and MoRAL score (obtained from the equation: $11*\sqrt{DCP}+2*\sqrt{AFP}$).

At ROC analysis, MoRAL score was the best predictor of: pathological major lesion >5 cm (AUC = 0.767; p-value < 0.0001), pathological Milan Criteria-OUT status (AUC = 0.681; p-value < 0.0001), satellitosis (AUC = 0.678; p-value = 0.001) and macrovascular invasion (AUC = 0.858; p-value = 0.001). AFP was the best predictor for poor grading (AUC = 0.846; p-value<0.0001) and microvascular invasion (AUC = 0.655; p-value = 0.001).

This study confirms in a European setting that the AFP/DCP combination strongly improves the ability to predict recurrence. DCP alone is a good marker of macrovascular invasion. AFP alone is an important marker of poor tumor grading and microvascular invasion. AFP/DCP combination is of paramount importance to determine HCC aggressiveness.

Basic Liver Biomarkers and molecular changes

BOS372 MULTIPLEX PCR SCREENING OF MICRORNAS IN GRAFT PRESERVATION FLUID DURING LIVER TRANSPLANTATION FOR BIOMARKER DISCOVERY

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Introduction: MicroRNAs (miRNAs) have been extensively investigated in recent years as biomarkers in liver transplantation. A variety of miRNAs in serum, tissue and bile have been demonstrated to correlate to rejection, early allograft dysfunction (EAD) and biliary complications after transplantation. However, the global miRNAs profiles in graft perfusion fluids during liver preservation have not been reported. In this study we aimed to identify miRNA profiles in graft perfusion fluids and investigate their potential to predict graft outcomes after liver transplantation.
Material and methods: Cell-free preservation fluids of 32 human liver grafts at the end of cold storage were analyzed for miRNA content using TaqMan microRNA array card A. 50% of grafts were from donation after brain death (DBD) and 50% from donation after circulatory death (DCD). For both donor types 8 grafts resulting in EAD and 8 resulting in non-EAD were included. Bioinformatics analysis was performed using the R-package HTqPCR normalized datasets.
Results: 220 miRNAs were reliably detectable in graft perfusion fluids. A difference in miRNA levels was seen between DCD and DBD livers for miR-523-3p, miR-525-5p, miR-382, miR-7a and miR-200a ($p < 0.01$). Furthermore, 11 miRNAs were identified as significantly different between EAD and non-EAD grafts (miR-491-5p, miR-200c, miR-382, miR-220, miR-221, miR-510, miR-542, miR-518b, miR-379 miR-204 and miR-122, $p < 0.01$). Graft perfusion fluids of liver grafts which developed biliary lesions after liver transplantation showed six new miRNAs (miR-455-5p, miR-191, miR-324-5p, miR-142, miR-302, miR-410, $p < 0.01$).
Conclusion: In this discovery study we have identified several new miRNAs in graft preservation solutions of liver grafts related to donor type and post transplantation graft function. Further research is ongoing to validate the use of these miRNAs to assess graft quality during preservation in a larger cohort.

Clinical Kidney Rejection

BOS373 NOVEL NON-INVASIVE BIOMARKERS DIAGNOSTIC OF ACUTE REJECTION IN THE TRANSPLANTED KIDNEY: A SYSTEMATIC REVIEW

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Background: Acute rejection (AR) is a significant complication detrimental to allograft function. Current accepted means of diagnosis is by percutaneous renal biopsy, a costly and invasive procedure. There is an urgent need to detect and validate non-invasive biomarkers capable of replacing the biopsy. This review aims to qualitatively assess the diagnostic performance of prospective biomarkers, discussing obstacles faced towards reaching clinical end points.
Methods: Comprehensive literature searches of Medline, EMBASE, Cochrane Central Register of Controlled Trials, PubMed and Ovid databases were performed. Eligible studies were included as per inclusion criteria and assessed for quality using the GRADE quality of evidence tool. Outcomes evaluated included diagnostic performance, number of patients/samples, mean age and gender ratio, in addition to clinical applications of the biomarker(s) tested. PRISMA guidelines were followed. Where possible, statistical analysis of comparative performance data was performed.
Results: 23 studies were included in this review, including 19 adult, 3 paediatric and 1 mixed studies. A total of 2858 participants and 50 candidate non-invasive tests were identified. Sensitivity, specificity and area under the curve performance values ranged from 36–100%, 30–100% and 0.55–0.98 respectively.
Conclusions: Although larger, more robust multi-centre validation studies are needed before non-invasive biomarkers can replace the biopsy, numerous candidate tests have demonstrated significant promise for various facets of post-operative management. Suggested uses include: ruling out patients with a low risk of AR to avoid the need for biopsy, non-invasive testing where the biopsy is contraindicated and a prompt diagnosis is needed, and integration into a serial blood monitoring protocol in conjunction with serum creatinine.

Clinical Kidney Biomarkers and molecular changes

BOS374 THE ROLE OF URINARY CHEMOKINES IN DISTINGUISHING CAUSES OF RENAL ALLOGRAFT DYSFUNCTION

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Body: Aetiology of renal transplant dysfunction is varied and diagnosis often relies upon renal biopsy, an invasive procedure that carries significant risk. Availability of a reliable, non-invasive test to determine the cause of graft dysfunction and facilitate longitudinal monitoring of an individual patient is therefore of significant clinical interest.

Recent studies have shown that levels of urinary chemokines may distinguish causes of allograft dysfunction, and, furthermore, correlate with long-term graft function. We have previously shown that urinary levels of osteoprotegerin (OPG), monokine induced by interferon-γ (MIG) and interferon-induced protein-10 (IP-10) were significantly higher in patients with acute rejection compared to controls. In this study, we extended the analysis to renal transplant patients with quiescent graft function or allograft dysfunction, including patients with ATN, rejection, BKV infection and those with an index of chronic damage (ICD) >20%.
Method: 360 urine samples were collected prospectively from 133 patients undergoing a protocol or clinically indicated biopsy, including 27 patients with rejection, 7 with BK viraemia/viruria, 18 with ATN, 27 with ICD >20% and 54 controls. Samples were analysed in duplicate using the Life Technologies™ Invitrogen™ Plexmark® 3 Renal Biomarker Panel kit.
Results: As shown in Table 1, there were significant differences in the mean levels of IP-10, OPG & MIG between groups.

There were also significant differences in each of the chemokines when pairwise comparisons were made according to diagnoses, particularly when comparing controls to those with rejection or BKV infection. There were no significant differences in the levels of any chemokine when patients with rejection were compared to those with BK infection, but it was possible to distinguish patients with ATN or an ICD >20%. These data support accumulating evidence that urinary biomarkers are a useful, non-invasive tool in diagnosis of graft dysfunction.

Clinical Kidney Other

BOS375 RENAL ALLOGRAFT TRANSPLANTECTOMY: MORBIDITY, MORTALITY AND IMPACT ON ALLOIMMUNIZATION ABOUT 180 CASES

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Background: Number of unfunctional kidney graft is actually growing up. 10% of patients returning to dialysis have still a non-functional graft. Role of renal transplantectomy and allo-immune impacts are poorly understood.
Material/Methods: This retrospective monocentric study of 180 transplantectomy was conducted from the first January 2000 to the 31 may 2015. Data were collected retrospectively and analyzed with statistical software SPSS 19.
Results: Population was 48.3% female and 51.7% male. The average age was 48 $\pm$ 15 years (7–76). The average running time of the kidney graft was 5.89 years (0–25.57).

38.33% of procedures were made by extracapsular approach and 61.67% by intracapsular.

Transplantectomy were perform for: graft intolerance syndrome 47.2%, graft infection 22.2%, artery or vein thrombosis 15.5% and tumor 8.33%.38.33% of procedures were perform in extra capsular approach in intracapsular way. The surgery time was 84.13 $\pm$ 40.12 minutes. Blood loss were 258.10 $\pm$ 601.32 ml. Morbidity was evaluate at 38% and mortality at 2.79%.

Complications was higher in surgery perform after 12 month ($p = 0.006$). Complications were also more important in several risky indications such as sepsis, venous/arterial thrombosis, non primary graft function, and kidney transplant removal in order to make space ($p < 0.05$) It has not been demonstrated significant difference in the evolution of anti-HLA antibodies according to the technique, based on transfusions, or for different groups of

patients transplanted or not. At the end of more than half of patients re-enrolled study on the waiting list were transplanted. The average time for the new transplant was 28.1 months (1.8–95).
Conclusion: Transplantectomy is a highly morbid procedure. It must be considered after optimizing anesthesiologic patient conditions. It must be done away from a septic episode which increases the complications and mortality.

BOS376 ARTERIOVENOUS GRAFT PLACEMENT AMONG PREVALENT HEMODIALYSIS PATIENTS WITH FAILED KIDNEY TRANSPLANTS: RESULTS FROM THE UNITED STATES RENAL DATA SYSTEM

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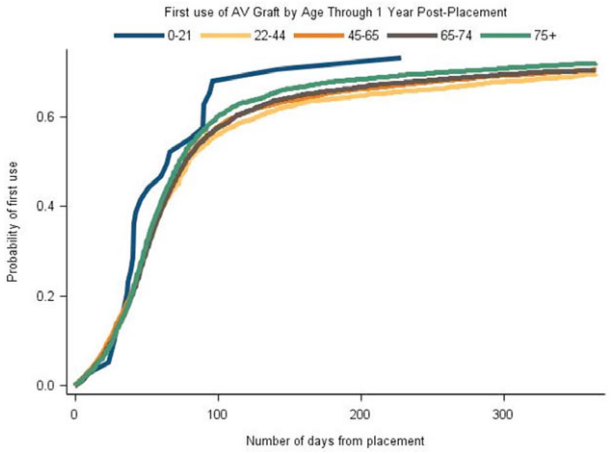
Kidney transplant patients with failed allografts returning to dialysis have substantial difficulty establishing access and are more likely to suffer from dialysis catheter (CVC)-related complications. The recent addition of Consolidated Renal Operations in a Web-Enabled Network (CROWNWeb) data to the United States Renal Data System (USRDS) allows more granular analysis of dialysis care parameters, including vascular access use. We've previously shown that 34% of arteriovenous fistulae (AVF) fail to mature in patients on HD with failed kidney transplants. Herein, we sought to explore the national experience in such patients receiving arteriovenous grafts (AVG).
Methods: We examined prevalent hemodialysis patients with previous failed kidney transplants within the last 3 years who had new AVG placements during 2013 using Medicare claims. Failure of maturation was identified by non-use following placement using CROWNWeb, where patient access use was reported monthly by the facility. Patients were followed until the end of 2014.
Results: Nationally, there were 688 patients who received AVG, compared to 1002 contemporaneous patients who received AVF. Of the AVG patients, there were 52% male, 44% Black, 41% White, and 7% Hispanic. The remaining were Asian, Native American, or of unknown race. Median time to first use of successful AVGs was 55 days (IQR 36–90 days), with 24% of placed AVGs with no record of use during the study period. Time to first use by age categories is shown in the Figure.
Conclusions: We have characterized AVG placements in patients with failed kidney transplants in a national US sample. AVG have a surprisingly high failure rate. Research is urgently required into the importance of patient, region, and practice factors that could decrease CVC use by improving AVF and AVG placement and maturation.



BOS377 SUCCESSFUL KIDNEY 7TH TRANSPLANTATION: A CASE REPORT

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Background: Retrospective analysis of a single case of 7th kidney transplantation (KTX) concerning the feasibility and efficiency in the light of organ shortage.
Methods/Materials: A male patient suffering from aplasia of the right and hydronephrosis of the left kidney underwent 1st KTX at age of 11 years (infantile donor, graft loss for CMV nephritis at month 11, in situ), 2nd KTX at 15 years (ATG; graft loss for chronic rejection at month32, explanted), 3rd KTX at 22 years (graft loss at week 1 for venous thrombosis; explanted), 4th KTX at 23 years (OKT III; graft loss for BK-nephropathy at month 1, explanted), 5th KTX at 25 years (immediately explanted for non perfusion due to cardiac arrest: successful resuscitated), 6th KTX at 26 years (Alemtuzumab, Rituximab; graft loss for chronic rejection at month47, in situ). Immunized by PRA 22% he underwent 7th KTX at 34 years, receiving a 17 years old donor kidney (HLA-MM: 1-1-1; cold ischemia 14:03 hours; ATG + Tacrolimus + MMF + Steroids).
Results: A reversible initial delayed graft function requiring 2 dialysis followed by a biopsy proven acute antibody mediated rejection reversed by 10 immunophoresis, resulted in a good graft function at actually month 24 within serum creatinine 1.1 mg/dl, DSA 0%, immunosuppression by low dosed Tacrolimus + MMF + steroids, good quality of life without serious adverse events or infections. No surgical complication occurred apart from a postoperative haematoma.
Conclusion: In the light of organ shortage and the knowledge of the extensive challenge concerning the immunological, surgical and infectious risk a 7th KTX should be evaluated very critically. This exceptional case of a successful 7th KTX was feasible due to the relatively low preceding immunization after totally 2/7 immunological graft losses, detailed knowledge of the patients history, exact monitoring of renal function and dosage of immunosuppression within multidisciplinary cooperation, good patient/familial adherence.

BOS378 CADAVERIC KIDNEY TRANSPLANTATION FOR A PATIENT WITH SUPER LONG-TERM PERITONEAL DIALYSIS OVER 19 YEARS: A CASE REPORT

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Encapsulating peritoneal sclerosis (EPS) is a severe complication of long-term peritoneal dialysis (PD) patients and may present after kidney transplantation, a condition known as posttransplantation EPS (PT-EPS). Due to risk of PT-EPS, there is no report of kidney transplantation for patient with super long-term (>15 years) PD duration. Here we report a patient who underwent cadaveric kidney transplantation at 19th year after starting peritoneal dialysis. The case was a 46-year-old Japanese woman with no history of PD-associated peritonitis and ultrafiltration failure. Cadaveric kidney transplantation was performed from a 56-year-old male cardiac death donor. Thickening of peritoneum specific to pre-EPS was not observed macroscopically. Postoperative course was uneventful, and she has not developed PT-EPS for two years from operation to the present. Peritoneal biopsy specimen collected at the operation showed a slight thickening of submesothelial compact zone (SCZ) without severe fibrosis and capillary occlusion. The average thickness of SCZ and the lumen/vessel diameter ratio at postcapillary venule were almost equivalent with those from only 4 to 8 years of PD duration. Peritoneal biopsy seems useful for evaluating the risk of EPS, so we recommend to collect peritoneal biopsy specimen at the operation from patients with long-term PD duration. PT-EPS may not need to be overly concerned about if there are no findings of severe peritoneal deterioration, such as capillary occlusion or severe thickening and fibrosis of SCZ.

BOS379 RENAL TRANSPLANTATION FROM A LIVING DONOR TO AN ADULT RECIPIENT: OUTCOMES AND RISK FACTORS

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Background: The living kidney transplantation is the best therapeutic alternative of end-stage chronic renal failure. However certain factors may affect the recipient and the graft survivals. What were the results of a renal transplantation from a living donor? And what would be its prognosis factors? Were the main objectives to unveil during this present study.
Methods: We retrospectively analysed data from 89 adult patients who underwent a living renal transplantation between January 2003 and December 2012 at the kidney transplantation unity in the Military Hospital of Tunis. Patients were followed-up at least for 2 years. Prognosis factors were identified through univariate and Cox multivariate regression analysis ($p < 0.05$).
Results: No death has been reported during the early phases and only one patient has lost his graft. 9 patients had vascular complications. 13 patients had urologic complications. 8 patients had a delayed graft function and 16 had an early acute rejection. An early infection was noted in 50.5% of the patients.
In late stage, 8 patients died (Survival rate was respectively 96.6% and 95.5% at 1 and 2 years). Only one patient has shown renal artery stenosis and 10 patients had urologic complications. 13 patients had lost their grafts

(respective Graft-survival at 1 and 2 years: 96.6% and 94.4%). 17% had acute rejections and 10% a chronic allograft nephropathy. 45% had infectious complications. 2 recipients have presented neoplasia. Predictive facts of unfavorable survival rate were the following: obesity, smoking, recipient's age >50 years and neoplasia. Obesity, black race, therapeutic non-compliance, early acute rejection, chronic allograft nephropathy, the MMF-Tacrolimus association and creatinine clearance at one year>60 ml/min/1.73 m^2 were the prognostic factors of the graft's survival.
Conclusion: According to our results, certain factors must be controlled mainly obesity, active smoking and therapeutic non-compliance to enhance patients and grafts outcomes.

BOS380 POTENTIAL IMPACT OF ARTERIOVENOUS FISTULA LIGATION ON KIDNEY TRANSPLANT OUTCOMES

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Serum Creatinine (mg/dl)	Previous to closure	1 month	6 months	12 months
AVF closure	1.03 ± 0.85	1.49 ± 0.82*	1.38 ± 0.78*	1.17 ± 0.87
Without AVF closure	1.71 ± 0.76	1.73 ± 0.76	1.77 ± 1.07	1.61 ± 0.70

*p<0.01.
Introduction: Routine closure of arteriovenous fistula (AVF) after renal transplantation is not recommended. However, it has been reported that closing AVF may have cardiovascular benefits. Recent studies have described an accelerated deterioration of graft function after this surgery. The aim of our study was to assess if surgical closure of AVF may affect kidney function and patient survival.
Methods: We identified patients who underwent AVF ligation after receiving a kidney transplant, and compared with a control group matched by gender, donor and recipient age, and transplant vintage. We prospectively analyzed kidney function before surgical closure and at 1, 6 and 12 months after the intervention, and compared with the control group the graft function and long-term failure as well as the possible impact in patient survival.
Results: We included 49 patients and 49 matched controls (1:1). 76.8% were males. Median time from AVF creation to AVF ligation was 8.33 (range 4.98–13.95) years. Mean age at transplantation was 45.6 ± 13 years and median time from kidney transplant to AVF surgical closure was 6.96 (range 2.62–11.97) years. We observed a decline in graft function after one ($p < 0.001$) and 6 months ($p = 0.002$); however, renal function returned to baseline at 12 months ($p = 0.264$) (table 1).
Long-term patient and graft survival, censoring and uncensoring by patient's death, was similar in both groups.
Conclusion: Surgical closure of arteriovenous fistula after renal transplantation is associated with an early transient worsening of graft function. However, this deterioration is reversible and does not affect long-term graft or patient survival.

BOS381 RISK OF VASCULAR COMPLICATIONS AND GRAFT LOSS FOR PATIENTS RECEIVING LIVING DONOR KIDNEY ALLOGRAFTS WITH MULTIPLE ARTERIES

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Background: The universal shortage of kidney grafts required to extend criteria of selection of donors as well as recipients. Thus, the use of living grafts with multiple arteries has considerably increased. As the innocuity allografts with complex vascular anatomy was controverted, we aimed to determine the rate of arterial reconstruction in our experience and to relate this to the occurrence of vascular complications and the risk of graft loss.
Methods: A series of 89 living renal transplantations performed between January 2003 and December 2012 at our unity of kidney transplantation was analysed with a mean follow-up time was 71.62 ± 34.47 months. To restore the arterial continuity, we have chosen to resort to the external iliac artery or the iliac bifurcation with an end-to-side anastomosis and the internal iliac artery with a side-to-side anastomosis.
Results: 23 donors (24.7%) had multiple arteries (14 allografts had 2 arteries, 9 allografts had 3). Grafts with 2 renal arteries have undergone an arterial reconstruction through a side-to-side joint "artery-to-artery" anastomosis in 4 cases and an end-to-side anastomosis of the accessory artery to the main one in 10 cases. For those with 3 renal arteries, we connect end-to-side the 2 accessory arteries to the main one.
Overall, 11 vascular complications were recorded. Renal artery stenosis occured in 4 patients. Otherwise, we didn't report neither renal artery nor venous thrombosis. In univariate analysis, patients receiving grafts with multiple arteries didn't face a statistically higher risk of vascular complication compared to those receiving grafts with single arteries (17% vs. 10% respectively p: 0.660). Additionally, univariate analysis has not shown any significant association between vascular reconstruction and graft loss (p: 0.185).
Conclusion: We concluded that there was no adverse impact of arterial reconstruction in the graft outcomes. Thus, complex vascular anatomy should not be a contraindication to renal transplantation.

BOS382 MACROSCOPIC ARTERIOSCLEROSIS OF THE RENAL ARTERY IS ASSOCIATED WITH PRIMARY NON-FUNCTION, BUT NOT WITH GRAFT FUNCTION OR LONG TERM SURVIVAL OF 50+ DECEASED DONOR KIDNEYS

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Introduction: The average deceased donor today is significantly older than donors were a few decades ago. Older donors have more arteriosclerosis of the renal artery. During organ retrieval, surgeons estimate the degree of arteriosclerosis and this plays an important role in decisions on organ acceptance. Our study aimed to elucidate the association between renal artery arteriosclerosis and transplant outcome.
Methods: Data from the Dutch Organ Transplantation Registry were used. We selected all renal transplants between 01-01-2000 and 31-12-2015, from deceased donors aged 50 years and older, carried out in any of the 8 transplant centres in The Netherlands. We included only those for which data on renal artery arteriosclerosis were available ($n = 2239$). Donors were either DBD ($n = 1107$) or controlled DCD ($n = 1132$). The association between arteriosclerosis and outcome was explored by means of multivariable logistic or linear regression and with multivariable Cox regression for survival data.
Results: Median donor age was 60 (range 50–82). Degree of arteriosclerosis was either none, mild, moderate, or massive ($n = 701$, 203, 1036 and 299, respectively). Arteriosclerosis was not significantly associated with delayed graft function (OR 1.16 95% CI 0.94–1.43 $p = 0.16$), eGFR 1 year post-transplant (B 0.58 95% CI −2.07 to 3.22 $p = 0.67$) and long term death censored graft survival (HR 1.07 95% CI 0.86–1.33 $p = 0.55$). There was a significant association between arteriosclerosis and primary non-function (7.3% vs. 5.3%, OR 1.60 95% CI 1.07–2.42 $p = 0.02$). A higher degree of arteriosclerosis did not make this association stronger.
Conclusion: Any macroscopic arteriosclerosis of the renal artery resulted in more primary non-function. Arteriosclerosis had no effect on delayed graft function, eGFR at 1 year, or long term graft survival. These data suggest that, if a 50+ deceased donor kidney shows immediate or delayed function, renal artery arteriosclerosis will not negatively affect transplant outcome.

BOS383 SINGLE CENTRE EXPERIENCE WITH A 3RD KIDNEY TRANSPLANT

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Introduction: Kidney transplantation has clear patient survival and quality of life advantages compared to dialysis. However, there are clear surgical and immunological challenges with multiple transplants; we reviewed the experience of our centre with 3rd kidney transplants.
Methods: 17 3rd kidney transplants that were performed from 2005 to 2016 were analysed retrospectively. There were 12 male and 5 female patients and the average recipient age at the time of the 3rd transplant was 43 years (29–63). There were 6 transplants from living (one was HLA incompatible) and 11 from deceased donors.
Results: In total 4 kidneys (24%) were lost, 2 (12%) due to thrombosis, 1 (6%) due to recurrent FSGS and 1 (6%) due to chronic antibody mediated rejection (CAMR).
6 patients (35%) experienced rejection but only one kidney was lost due to CAMR.
One patient developed an infected peri renal collection that was treated conservatively. One patient developed a myocardial infarction due to re-stenosis in previously placed coronary stent, treated with percutaneous intervention (angioplasty + stent).
The patient who lost the kidney for renal venous thrombosis, had also bilateral iliac veins thrombosis extending into lower IVC. He never had in the past DVT/PE. The patient who lost the kidney for recurrence of FSGS required an IVF filter, 7 months after the tx, for new acute distal DVT (old chronic femoral DVT). We had 3 cases of new onset of Diabetes after the 3rd tx.

The 1 year patient and graft survival were 100% and 81.5% respectively. The mean creatinine at 1 year was 134 μmol/l. For the same cohort of patients the mean follow up was 59 months (range 19–120) and the patient and graft survival were 97% and 75% respectively. The mean creatinine at 59 months was 162 μmol/l.
Discussion: Our results confirm that a 3rd kidney transplant is a valid therapeutic option with very satisfactory short and long term outcomes.

BOS384 INCIDENCE, RISK FACTORS AND IMPACT ON LONG-TERM OUTCOMES OF LYMPHOCELES IN KIDNEY TRANSPLANTATION

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Introduction: Despite preventive methods, lymphoceles (Lc) are common complications after kidney transplantation in about a third of patients (pts).
Methods: In this retrospective single center study 873 adult pts, who received cadaveric or living donor kidneys from 2006–2015, were included. All pts with diagnosis of Lc and necessity of intervention were identified and analyzed.
Results: 307 (35%) pts with lymphoceles were identified with a median time of diagnosis of 29 days (IQR 19–51) post-transplant. 72 (8%) patients needed intervention, which was performed 22 days (median, IQR 8–55) after diagnosis. Incidence of Lc formation and time of intervention are shown in figure 1a. 81.9% of the interventions were laparoscopic fenestrations. The remainder received a drainage (13.9%) or open surgery (4.2%).

In our cohort, Lc was significantly associated with old age, long cold ischemia time, deceased donors, T-cell mediated rejections ≤30 days after tx (TCMR30), DGF and the donor risk factor bundles KDPI/living KDPI in the univariate logistic regression model. Multivariate analysis, adjusted for all relevant factors, revealed living donation as protective factor (OR 0.54, $p < 0.001$) and TCMR30 as independent risk factor (OR 1.61, $p = 0.001$) for lymphocele formation.

Comparison of patients with conservatively treated lymphoceles versus lymphoceles with interventions versus controls revealed no difference in death censored graft survival (74.5% vs. 85.5% vs. 75.7%, figure 1b) or patient survival (67.8% vs 72.5% vs. 67.1%, figure 1c) over 10 years. An adjusted multivariate analysis confirmed that lymphocele interventions did not increase the risk for premature graft loss (HR 0.57, $p = 0.126$).
Conclusion: Lymphoceles occur frequently after transplantation, the majority within the first 50 days post-transplant and are independently linked with early T-cell mediated rejections. Development or intervention of lymphoceles did not lead to poorer graft survival.

BOS385 IS THE VARIABILITY OF RENAL ARTERIAL RESISTANCE INDEX MEASUREMENTS USEFUL PARAMETER OF LATE GRAFT FUNCTION AFTER RENAL TRANSPLANTATION?

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Background: The influence of RI after renal transplantation on its predictive power has not been sufficiently evaluated. We performed retrospective analysis of RI and its power to predict renal allograft failure or death with special emphasis on the time point and the variability of RI measurements.
Methods: RI measurements were obtained from 107 transplanted patients on POD 1 and POD 7 from January 2000 to November 2013. All patients with RI measurements were retrospectively stratified into three groups according to the RI value; Group 1: index of <0.70 ($n = 73$ (68.2%) on POD 1 and $n = 82$ (76.6%) on POD 7), Group 2: index between 0.70 and 0.85 ($n = 30$ (28.0%) on POD 1 and $n = 22$ (20.6%) on POD 7), and Group 3: index of ≥ 0.85 ($n = 4$ (3.7%) on POD1 and $n = 3$ (2.8%) on POD 7). The graft function of kidney was estimated.
Results: RI at POD 7 showed a significant predictive value for renal transplant failure or death in a univariate approach [$p = 0.0001$]. Patients with the Group 3 on POD 7 showed the highest incidence of DGF [$p = 0.0001$], eGFR[median value = 17.00, $p = 0.004$] and s-Cr[median value = 5.20, $p = 0.0001$], among three groups. The analysis of the change in RI value showed that the increased RI index between POD 1 and POD 7 was significant for a dismal outcome; DGF [$p = 0.0001$]. Survival analysis of each three group on POD 7 was as in the following; acute rejection episodes: 4.1% ($n = 3$) in Group 1, 13.3% ($n = 4$) in Group 2, 25% ($n = 1$) in Group 3 and incidence of DGF: 1.3% ($n = 1$) in Group 1, 6.6% ($n = 2$) in Group 2, 100% ($n = 4$) in Group 3 and during follow up period 13 graft losses occurred in patients.
Conclusion: RI measurements on 7 days after transplantation appeared useful to predict allograft outcomes. Sequential renal duplex ultrasonography can be useful for identifying high risk group for subsequent development of graft failure.

BOS386 THE IMPACT ON KIDNEY FUNCTION OF THE RENAL RESISTIVE INDEX IN THE IMMEDIATE POSTOPERATIVE PERIOD AFTER KIDNEY TRANSPLANTATION: A COHORT ANALYSIS

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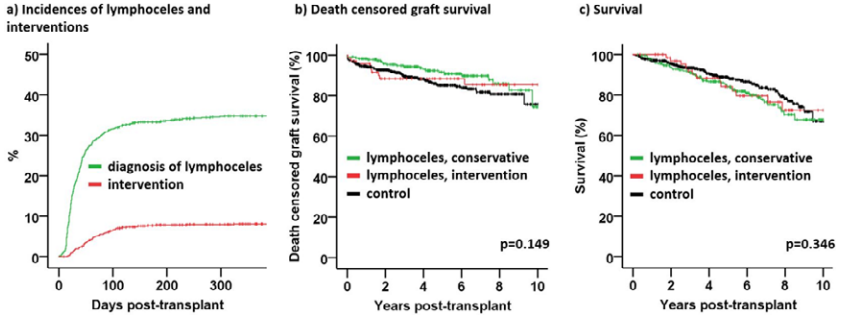
Background: The renal resistive index (RI) is in our hospital routinely used for the clinical monitoring of the transplanted patients in the very early postoperative period. It is a non-invasive method that allows us to detect microvascular changes in intrarenal arterial blood flow. The aim of this study was to determine whether the RI measured in the immediate post-transplant phase during ICU admission can be used to predict short-term graft function.
Methods/Materials: We performed a retrospective study in one tertiary care academic center. We included kidney transplant recipients who were transplanted between 2005 and 2014 and who had RI measured by Doppler ultrasonography within the first 2 days after kidney transplantation. Short-term outcome (measured up to 10 days) was studied by 22 different definitions of delayed graft function (DGF). Donor, recipient and outcome variables were retrospectively retrieved from the electronic hospital database, the laboratory database, DICOM images, the database on intensive care (Adaptive Server Enterprise), the database of our Transplantation Center, the Eurotransplant database and local databases of peripheral hospitals.
Results: We included 446 recipients, of which 279 (62.6%) were male, with a median age of 55 years (IQR 46–63). Median cold and warm ischemia time were respectively 13.6 hours (IQR 10.5–16.7) and 20.0 minutes (IQR 17.0–24.0). Median RI was 0.62 (IQR 0.55–0.70). Depending on the definition used, DGF was present in 4.4–41.7% of recipients. We found that for most of the DGF definitions studied, RI was higher in patients who had DGF.
Conclusion: DGF was associated with an increased RI already within the first 2 days after kidney transplantation.

Figure 1



BOS387 IMPACT OF THE KIDNEY DONOR PROFILE INDEX (KDPI) ON GRAFT SURVIVAL IN SOUTHERN EUROPEAN DECEASED DONOR KIDNEY TRANSPLANT

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Objective: To evaluate the association between KDPI and graft survival in Southern European deceased donor kidney transplant recipients (DKT).
Methods: A longitudinal, retrospective cohort study, where were included 733 DKT performed in our center (Carlos Haya Hospital, Málaga, Spain) during 1999–2012. KDPI was calculated in all deceased donors.
Results: Recipient's mean age was 49 ± 13 years and 61.1% were male. Mean dialysis time was 38 ± 35 months. 85% was the first transplant. Donor's mean age was 49 ± 17 years, and hypertension and diabetes was present in 31.7% and 12%, respectively. Stroke was the cause of donor death in 61%. Cold ischemia time (CIT) was 15 ± 4 hours and 41% of patients had delayed graft function. The most commonly used immunosuppressive treatment was steroids, MMF and Tacrolimus (88%). Induction therapy (46.4% anti-CD25, 14.4% thymoglobulin) was administered in 61% of patients. A total of 150 patients (17%) lost the graft during follow-up (96 ± 58 months).

Median KDPI was 63 (IQR 34–86). Patients were divided into 2 categories: KDPI≤80 (502 patients) and KDPI>80 (231 patients). Donors with KDPI>80 were older (65 ± 7 vs. 41 ± 14 years; $p < 0.001$), and had more hypertension (63% vs. 16%; $p < 0.001$) and diabetes (26% vs. 5%; $p < 0.001$). The patients who received a kidney with KDPI>80 also were older (60 ± 8 vs. 45 ± 13 years; $p < 0.001$) and had a higher proportion of diabetics (14% vs. 7%; $p = 0.001$). There were no differences in CIT (15.6 ± 4.2 vs. 15.2 ± 4.6; $p = 0.3$). Overall graft survival at first, 5th and 10th years was significantly lower in patients with KDPI>80 vs. ≤80 (88%, 74%, 52% vs. 91%, 83%, 70%, respectively; $p < 0.001$), as well as patient death-censored graft survival (91%, 83%, 71% vs. 93%, 87%, 80%; respectively, $p = 0.03$). In multivariate cox regression analysis, a KDPI value (≤o > 80) was significantly associated with graft failure (HR 1.9; 95% IC 1.1–3.3; $p = 0.009$).
Conclusions: A KDPI value >80 represents an important risk factor for graft loss in our kidney transplant population, with an increased of risk of 1.9 times.

BOS388 UNDERSTANDING LATE KIDNEY TRANSPLANT FAILURE: IS "DEATH WITH A FUNCTIONING GRAFT (DWF)" REALLY DEATH WITH FUNCTION?

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To understand causes of kidney transplant (KT) failure, outcomes are often segregated into death censored graft failure (DCGF, a proxy for immunologic injury) and DWF. To define whether these categories actually represent distinct entities, we examined clinical course and the change in kidney function (slope of 1/Cr) from 3-months post-transplant (baseline) among 3719 DeKAF study participants from seven centers followed prospectively from transplant (2005–11) for a median of 5.4 years. 3 groups were defined by outcome event: death (DWF), graft failure (DCGF), or neither (maintained function, MF).

	DWF	DCGF	MF	p
N	360	312	3047	
Age at KT, mean (SD)	56.8 (12.4)	42.2 (14.7)	48.9 (14.7)	<0.001
Race (% African American)	20.6	31.8	15.8	<0.001
Yrs on dialysis, median (IQR)	2.1 (0.4, 4.9)	1.6 (0.3, 4.8)	1.0 (0, 3.0)	<0.001
Delayed graft function (%)	14.3	15.1	6.6	<0.001
AR before month 3 (%)	7.8	15.4	6.7	<0.001
Yrs to event (after month 3), mean (SD)	3.3 (2.0)	3.0 (1.8)	NA	0.14
Baseline serum Cr, mean (SD)	1.4 (0.5)	1.7 (0.8)	1.4 (0.4)	<0.001
Slope* (dl/mg/year)	−0.018	−0.097	−0.005	<0.001

*From a random effects model with fixed effects for event type, time, and their interaction and random intercept with compound symmetry correlation structure. Excluding serum Cr values within 2 weeks of graft failure did not qualitatively change findings.

Patients with DCGF were younger at KT, more likely AA, and more likely to have had early AR, demonstrating a significantly greater slope of decline in 1/Cr before DCGF than DWF or MF (−0.097 vs. −0.018 or −0.005). Among those with DWF, 69% had a final serum creatinine value ≤2.0 mg/dl, and only 6.5% were >4.0 mg/dl. Those with DWF were older at KT and had lengthier time on dialysis, but similar incidence of early AR, baseline renal function, and slope beyond day 90 as those with MF. DWF and DCGF represent two distinct adverse outcomes after KT, and patients with DWF maintain stable graft function, comparable to those with excellent outcomes, prior to terminal event.

Clinical Liver Other

BOS389 THE OUTCOMES AND INDICATIONS OF ENDOVASCULAR STENTING FOR VENOUS COMPLICATIONS FOLLOWING PEDIATRIC LIVER TRANSPLANTATION

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Background: With respect to portal vein (PV) or hepatic vein (HV) complications following pediatric living-donor liver transplantation (LDLT), while advancements in interventional radiology (IVR) treatment have significantly improved its prognosis, it may develop into graft failure at worst. Intravascular stent placement and surgical re-anastomosis are considered for refractory cases, with the indications remaining controversial. We herein show the outcomes of intravascular stent placement for venous complications at our department and discuss regarding the optimal indications.
Method: The subjects consisted of 282 patients who underwent pediatric LDLT at our department from May 2001 to September 2016. Patients with PV or HV complications underwent surgical or IVR treatments, while recurrent and refractory cases were considered for intravascular stent placement.
Results: HV complications were observed in 22 patients (7.8%). Among which 9 patients (40.9%) underwent several times of IVR treatment, 2 patients of them (9.1%) underwent intravascular stent placement. The frequency of IVR treatment prior to stent placement was once and eight times, with a stent placement duration of 9 months and 46 months following LDLT. Both patients caused thrombotic occlusion (14 months later, 8 months later), therefore re-transplantation was indicated in them. PV complications were observed in 40 patients (14.2%). Among which 10 patients (25.0%) underwent several times of IVR treatment, 4 patients (10.0%) of them underwent intravascular stent placement. The median duration of stent placement was 11 months (6 months to 3 years). All 4 patients are patent with an average duration of stent patency of 43 months.
Conclusion: The treatment of intravascular stent placement is effective for PV complications following pediatric LDLT. On the other hand, the treatment of intravascular stent placement for HV complications should be carefully performed because of intrastent thrombus formation.

BOS390 CAN ROTATIONAL THROMBOELASTOMETRY PREDICT HAEMOSTATIC RESERVE IN PATIENTS WITH END-STAGE LIVER DISEASE UNDERGOING LIVER TRANSPLANTATION?

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Introduction: Patients with End-Stage Liver Disease (ESLD) are at high risk of both severe perioperative bleeding and thrombosis during the perioperative period of liver transplantation (LT). Rotational thromboelastometry (ROTEM) is extensively used for guiding transfusion during LT. Our aim was to assess whether derived ROTEM parameter can be used to assess haemostatic reserve in ESLD.
Methods: 176 patients undergoing LT between January 2013 and March 2016 were included. Demographic data, severity of ESLD (MELD score), standard coagulation tests (INR, aPTT, PT), fibrinogen levels, platelet count and ROTEM parameters were collected preoperatively. Four ROTEM tests were performed (ExTEM, InTEM, FibTEM, ApTEM) and the following parameters were recorded: standard parameters (clotting time-CT, clot formation time-CFT, maximum clot firmness-MCF) and derived (thrombin potential index-TPI, maximum velocity of clot formation-MaxV, time to MaxV-MaxVt, area under the curve-AUC and maximum clot elasticity-MCE). Intraoperative data consisted of: intraoperative blood loss and transfusion requirements (packed red blood cells–PRBc, fresh frozen plasma–FFP, platelet concentrates–PC).
Results: No statistical significant correlation was noted between intraoperative blood loss and standard coagulation tests but an increased MaxVt was

associated with increased blood loss (p = 0.005). Also MaxVt was associated with increased PRBc requirements (p = 0.047). FFP transfusion was significantly correlated with decreased InTEM TPI (p = 0.001) and ExTEM TPI (p = 0.001), decreased MaxV (p = 0.001) and decreased MCE (p = 0.001). Decreased InTEM TPI (p = 0.01) and ExTEM TPI (p = 0.03), decreased MaxV (p = 0.04) and MCE (p = 0.04) were significantly associated with PC transfusion.
Conclusion: Derived ROTEM parameters offer additional information on haemostatic reserve in patients with ESLD undergoing LT and represent good predictors of intraoperative blood loss and transfusion.

BOS391 THE ROLE OF PRE-TRANSPLANT TIPS IMPLANTATION IN ORTHOTOPIC LIVER TRANSPLANTATION

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Background: Portal hypertension and its complications such as variceal bleeding are one of the main causes of death on the liver transplantation waiting list. Transjugular portosystemic shunt (TIPS) implantation is used for treatment of several complications in patients with liver cirrhosis and has recently re-evolved as elegant therapeutic option. Recent studies have identified a survival benefit for patients on the waiting list after TIPS implantation but the optimal time point for TIPS implantation prior to orthotopic liver transplantation (OLT) has not been established.
Methods: We retrospectively assessed patients undergoing TIPS implantation before or after listing for OLT at our institution. We identified $n = 98$ patients with TIPS on the waiting list between JAN/1993-DEC/2013 ($n = 73$ (74.5%) pre-listing, $n = 25$ (25.5%) post-listing). A matched control group at the time of OLT without TIPS ($n = 60$) was included. The retrospective study was approved by the Medical University of Vienna's institutional review board (EK 2119/2015).
Results: More patients with post-listing TIPS (28.0%, 7/25) showed clinical improvement and went off-list than patients with pre-listing TIPS (8.2%, 6/73, p = 0.0119). A similar proportion of patients with pre-listing TIPS (19.2%, 14/73) and post-listing TIPS (20.0%, 5/25) died on the OLT waiting list. Transplant surgery time was similar in patients with/without TIPS: 348 (±13) vs. 337 (±10) minutes (p = 0.5139). Estimated 1-year post-transplant survival was similar across all groups (pre-listing TIPS: 76.2%, post-listing TIPS: 86.0%, no TIPS: 91.2%, log-rank p = 0.1506). Patients that were de-listed because of clinical improvement had similar survival rates to patients that underwent OLT.
Conclusion: TIPS does not complicate the liver transplantation procedure itself and should be considered in all liver transplant candidates since it can obviate the need for OLT and optimize bridging to OLT.

BOS392 EVALUATION OF ACOUSTIC RADIATION FORCE IMPULSE (ARFI) ELASTOGRAPHY AS NONINVASIVE DIAGNOSTIC TOOL IN LIVING DONOR LIVER TRANSPLANTATION

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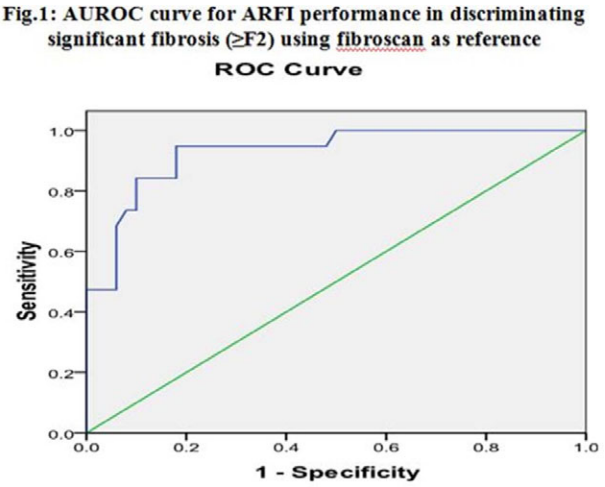
Background: Acoustic radiation force impulse (ARFI) elastography is an efficient non-invasive method for assessment of liver fibrosis. Yet, its role in the transplant setting is not well established. We aimed to evaluate ARFI elastography as predictor of graft fibrosis post LDLT and to compare it with other non-invasive methods (Transient Elastography [TE], APRI and FIB4).
Patients and methods: 70 recipients recruited from February 2015-September 2016. APRI and FIB4 scores were calculated for all recipients. TE and ARFI elastography were performed to all recipients. A minimum of 10 valid ARFI values were measured in the right liver lobe using a Siemens Acuson S2000 ultrasound system (Acuson, Siemens Medical Systems Co. Ltd. Erlangen, Germany). Only 30 recipients had liver biopsy due to graft dysfunction. Significant fibrosis was defined as ≥F2.
Results: The mean age of our cohort was 49.5 ± 8.49 years, 85.7% males, with mean BMI 26.2 ± 4.2 kg/m^2. Post hepatitis C cirrhosis was the commonest cause of LT (85.7%). Fibrosis stages<=“”>
Conclusion: Liver stiffness measurement by ARFI correlates well with TE and other non invasive fibrosis markers in post liver transplant. ARFI can be used as a reliable method in assessment of significant fibrosis post LDLT.

Fig.1: AUROC curve for ARFI performance in discriminating significant fibrosis (≥F2) using fibroscan as reference



BOS393 LONG-TERM OUTCOMES FOR LIVER TRANSPLANT RECIPIENTS IN TERMS OF HEPATIC ENCEPHALOPATHY

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Background: Liver transplantation (LT) is thought to resolve cognitive deficit due to hepatic encephalopathy (HE). The aim of this study was to determine the factors associated with the outcomes of patients with HE after LT.
Methods: The authors reviewed the medical records of 388 patients with HE who underwent LT from 1996 to 2014.
Results: There were 282 patients with grade 1–2 HE and 106 patients classified as grade 3–4. Patients in the latter group had a tendency for a more decompensated hepatic condition than patients with grade 1–2 HE. HE Sequelae were only associated with grade 3–4 HE with borderline significance (p = .05). The cumulative 1-, 3- and 5-year overall survival (OS) of patients with grade 1–2 HE were 81.9%, 77.3% and 74.6%, while those of in patients with grade 3–4 HE were 77.4%, 73.3% and 72.2%, respectively (p = .75).
Conclusion: The sequelae of HE were only associated with the grade 3–4 HE. Aggressive treatment of HE prior to LT may prevent patients from deteriorating into high grade of HE, which could further contribute to improving the outcomes after LT.

BOS394 THE CAUSES AND OUTCOMES OF EARLY RELAPAROTOMY FOLLOWING PAEDIATRIC LIVING DONOR LIVER TRANSPLANTATION

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Background: Although early relaparotomy of a recipient after living donor liver transplantation (LDLT) is significantly associated with poor prognosis, there are few reports limited to paediatric recipients. The aim of this study is to clarify the causes and outcome of early relaparotomy after paediatric LDLT.
Patients and Method: A total of 265 paediatric LDLT recipients (272 transplantations) transplanted from May 2001 to October 2015 were retrospectively analysed. Early relaparotomy was defined as occurring within 3 months after LDLT.
Results: Early relaparotomy was performed 49 times for 32 cases (33 transplantations, 12.0%). The causes of early relaparotomy were postoperative intra-abdominal hemorrhage (12 cases), vessel complications (12 cases), bowel perforation (9 cases), intra-abdominal abscess (7 cases), ileus (3 cases), secondary abdominal fascia closure (2 cases) and other causes (4 cases). Early relaparotomy was performed at 19.1 ± 19.1 postoperative days. The early relaparotomy group had a significantly higher PELD/MELD score (13.7 vs. 6.3, p = 0.0047), longer operation time (17 h 03 m vs. 14 h 46 m, p = 0.015) and greater bleeding volume (193.0 ml/kg vs. 99.4 ml/kg, p = 0.025) than the non-early relaparotomy group. The recipient survival rate and graft survival rate of the early relaparotomy group were 75.0% and 63.6%, respectively, compared to 96.6% and 95.8%, respectively, for the non-early relaparotomy group. Both measures were significantly lower (p < 0.001) in the

early relaparotomy group. Then, the relaparotomy group cases were divided into the infectious group and non-infectious group: the recipient survival rate was 50.0% in the infectious group and 86.7% in the non-infectious group ($p = 0.028$).
Conclusion: The recipient and graft survival rates were significantly decreased in the early re-laparotomy group. The risk factor of the early relaparotomy was pre-operative high MELD/PELD score. Especially, infectious complications such as bowel perforation and intraabdominal abscess lead to poor prognosis. In those cases, it needs early detection and treatment.

Clinical Liver Other

BOS395 SEVERITY OF POSTOPERATIVE ACUTE KIDNEY INJURY PREDICTS DEVELOPMENT OF CHRONIC KIDNEY DISEASE AFTER DCD LIVER TRANSPLANTATION

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Background: About 50% of the patients who receive a DCD graft develop acute kidney injury (AKI) after liver transplantation. However, the incidence and aetiology of chronic kidney disease (CKD) with the use of these high risk grafts remains less well defined. Our aim was to analyse the development of CKD in relation with postoperative AKI after DCD liver transplantation.
Methods: Two-center retrospective cohort study of all DCD liver transplantations (2001–2015). eGFR was calculated using the MDRD-4 formula and kidney function was divided into 3 groups: no CKD (eGFR $\geq$ 60), mild CKD (eGFR 30–59) and severe CKD (eGFR $<$ 30). Recipients who died or underwent retransplantation in the first 3 months after transplant were excluded. Postoperative AKI was defined according to KDIGO criteria.
Results: A total of 381 patients were included. The median pre-transplant eGFR was 100 (IQR 77–123) ml/min/1.73 m^2. Overall, 153 (40%) recipients developed CKD, but only 17 (5%) developed severe CKD. Four recipient required renal replacement therapy (RRT) and 1 recipient underwent kidney transplantation. The course of long-term kidney function after transplant is displayed in Figure 1. The majority of kidney dysfunction in the first week after transplant (61%) resolved in the first months, but kidney function slowly deteriorated afterwards. Multivariable cox-regression identified severity of AKI as an independent risk factor for the development of CKD: hazard ratio 1.51 (95% CI 1.01–2.28) for patients with AKI without RRT and hazard ratio 2.0 (95% CI 1.29–3.20) for recipients with AKI requiring RRT. Other independent predictors were recipient age, pre-transplant kidney function and female gender.
Conclusion: The majority of early kidney dysfunction after DCD liver transplantation resolves in the first months and the incidence of severe CKD after DCD liver transplantation is relatively low. However, the severity of postoperative AKI is an independent predictor of chronic renal impairment.

BOS396 SINGLE-CENTER EXPERIENCE OF ABO-INCOMPATIBLE LIVING DONOR LIVER TRANSPLANTATION WITH A SIMPLIFIED DESENSITIZATION PROTOCOL

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The outcomes of patients who undergo ABO-incompatible (ABO-I) living-donor liver transplantation (LDLT) have markedly improved as strategies have become more innovative and advanced. Here, we analyzed outcomes via a retrospective review of 50 ABO-I LDLTs in our institution from January 2011 to December 2016.

The basic desensitization protocol included plasma exchange, rituximab without local infusion therapy. From the 1st to 37th case, intravenous immunoglobulin (IVIG) was employed after LDLT on days 1, 3, and 5 for omitting graft local infusion (group I, $n = 37$). From the 38th case onwards, IVIG was eliminated from the protocol (group II, $n = 13$). The triple immunosuppression protocol consisted of tacrolimus and steroids with mycophenolate mofetil; a splenectomy was not routinely performed. Neither C4d staining nor clinical signs of antibody-mediated rejection was apparent in these cases. There were no significant differences in patient demographics or perioperative variables between the two groups except postoperative hospital stay (31.2 ± 11.0 vs. 24.9 ± 3.6, $p = 0.048$). Postoperative peak isoagglutinin (IA) titer, frequency of plasma exchange, and postoperative complications including diffuse intrahepatic biliary stricture were not significantly different between two groups. Moreover, no significant difference in overall or graft survival was observed between the groups.

In conclusion, ABO-I LDLT can be performed safely under new more simplified protocol and may be proposed when ABO-compatible donors are unavailable.

BOS397 DETERMINATION OF THE DIFFICULTIES, QUALITY OF LIFE AND SELF CARE ABILITY OF THE LIVER TRANSPLANTATION RECIPIENTS WHO LIVE AWAY FROM LIVER TRANSPLANTATION CENTER

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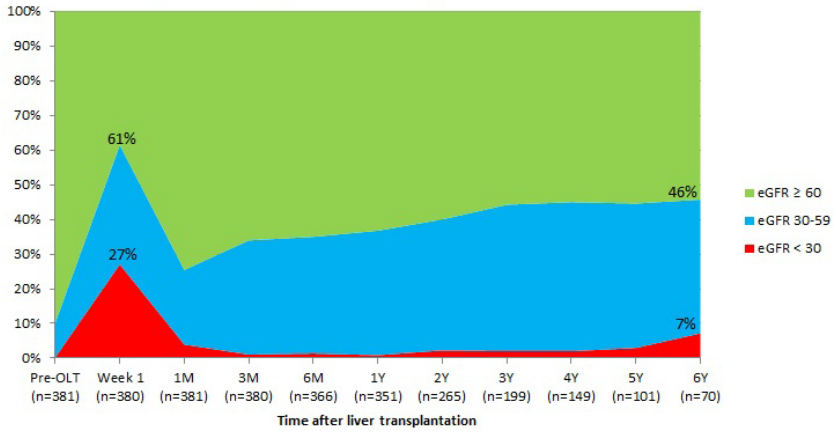
Aim: The purpose of this study was to investigate difficulties, quality of life, and self care ability levels of liver transplant recipients who live away from liver transplantation centers.
Materials and Methods: The research was made as a retrospective, descriptive and cross-sectional research design. The data of the research were collected in a province in the southeast of Turkey between December-March 2016. The data were obtained from 38 liver transplant recipients who live away from liver transplantation centers. To collect the data, the Patient Identification Form, SF-36, MTSOSD-58 and Self Care Ability Scale were used. For the analysis of the data, descriptive statistics (frequencies, mean and standard deviation), variance, correlation and ridit analysis were used.
Results: The mean age of the participants was 48.13 ± 12.90 years. It is found that recipients experienced very different difficulties related to hospital visit, financial, drug adherence, diet adherence etc. The transplant recipients'

Figure 1: long term kidney function after DCD OLT



physical and mental health scores of quality of life were found 35.84 ± 9.21, 36.48 ± 12.53 respectively. Their self care ability mean was determined as 106.55 ± 18.91. A strong and significant correlation in the positive direction was determined between the physical health score, the mental health score and the self care ability. Among the symptoms, the recipients experienced most was fatigue (ridit value = 0.72). It was determined that women experienced more symptoms than men ($p < 0.032$) according to the statistics.
Conclusion: In our study, it was determined that liver transplant recipients who live away from transplantation centers had many physical, psychological and social problems. Also, it was found that the quality of life of the liver transplantation recipients was low, their self-care ability was good and their symptom occurrence was high.

BOS399 VARIABLE DEFINITIONS OF NASH-RELATED CIRRHOSIS IN LIVER TRANSPLANT RECIPIENTS CHALLENGE THE ESTABLISHMENT OF STANDARDIZED GUIDELINES TO IMPROVE LOG-TERM SURVIVAL

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Background: Nonalcoholic fatty liver disease (NAFLD) and its progressive form, nonalcoholic steatohepatitis (NASH) have emerged as the most common liver disorders in the western world. Evidence-based guidelines to improve management of NASH related cirrhosis are rare and definition of NASH still vary in single-center studies.
Methods: Data from all deceased-donor liver transplants performed between 2002 and 2012 as recorded in the European Liver Transplant Registry were analyzed. NASH group as recorded in the database was compared to other established definitions of NASH including the NASH plus CC with a BMI >30 group, NASH plus 50% of CC. NASH groups were compared to the nonNASH cohort.
Results: Among the 37.612 adult LT cases, NASH comprised 0.9% (337). Female gender, gender mismatch, recipient BMI and donor steatosis stratified as steatosis to mild, moderate and severe did not impact on the outcome in the NASH patient group, while MELD score in NASH patients was significant ($p = 0.029$). The percentage of patients with advanced NASH was 3.3% (660/37612). Female patients and gender mismatch were identified as independent risk factors within the NASH cohort. The impact of donor age, recipient BMI and donor liver steatosis were significant in nonNASH, but not NASH patients ($p < 0.00$, $p = 0.01$, and $p = 0.01$). Donor BMI over 30 m^2/kg was identified as risk factor ($p = 0.023$). Within the NASH group plus 50% of CC recipient BMI, MELD, and donor age were independent risk factors. Overall survival was not significant in all three groups.
Conclusion: All three groups had different results regarding donor and recipient parameters. The implementation of international standardized definitions seems necessary in order to establish consistent evidenced-based guidelines.

BOS400 CHANGES IN INTRA-OPERATIVE TRANSFUSION PRACTICE OVER 8 YEARS IN LIVER TRANSPLANTATION

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Background: In liver transplantation (LT), the adoption of patient blood management strategies, including the utilisation of whole blood viscoelastic testing (VET) to guide transfusion, have contributed to a reducing need for allogenic blood products intra-operatively. It is recognised that 30% of LTs occur without the need for allogenic blood. We retrospectively audited our transfusion practice over an 8 year period.
Methods: A single centre retrospective case note review was undertaken in a total of 300 patients in three 100 patient cohorts spanning 2008–9, 2013–14 and 2015–16. Information was collected on intra-operative blood product usage. Intraoperative transfusion of autologous blood using cell salvage was standard practice through-out the cohorts. Data was analysed using Kruskal-Wallis test for non-parametric data and the two-tailed Chi-square test for categorical data.

Results:

	Group 1 2008–9 $n = 100$	Group 2 2013–14 $n = 100$	Group 3 2015–16 $n = 100$	p Value (statistical sig <0.05)
Median RBC (IQR)	2 (0–6)	3.5 (0–5.25)	2 (0–4)	0.70
Median FFP (IQR)	4 (2–6.25)	2 (0–5)	0 (0–4)	<0.001
Median platelet (IQR)	1 (0–2)	0 (0–1)	0 (0–1)	<0.001
>6 unit transfusion	27	26	15	0.14
Use of fibrinogen concentrate (median dose)	12 cases (2g)	26 cases (2g)	24 cases (2g)	
Use of prothrombin complex concentrate (median dose)	10 cases (1500 units)	19 cases (1500 units)	6 cases (1000 units)	
RBC-free LT	31	31	29	0.96
FFP-free LT	21	42	63	<0.001
Platelet-free LT	40	61	67	0.02
Cryoprecipitate-free LT	66	95	98	0.02

Median RBC transfusion (2 units) has remained consistently low over the years, the narrowing interquartile range indicating more consistent transfusion practice around the median. A significant reduction in the intra-operative administration of FFP and platelets was demonstrable with more product-free LTs taking place in the later cohorts. The increased use of fibrinogen concentrate was associated with a significant rise in cryoprecipitate-free LTs between 2008–9 and 2013–14. As expected, 30% of all transplants in each cohort occurred without the need for allogenic blood. A declining trend in the rate of massive transfusion (>6 units) was seen although statistically non-significant.
Conclusions: Multiple advancements in liver transplantation including, but not limited to, the utilisation of VET with avoidance of empirical management of coagulopathy, have led to a sustained decline in intra-operative blood product usage within our centre. Massive transfusion is difficult to mitigate and remains a significant threat due to the nature of surgery.

BOS401 THE REAL INCIDENCE OF BILIARY TRACT LESIONS (BTLS) AFTER LIVER TRANSPLANTATION (LT): THE ROLE OF A PROSPECTIVE ROUTINE USE OF DELAYED CHOLANGIOGRAPHY

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Background: The incidence of BTLs after LT is often underestimated due to their frequent silent behavior. The purpose of this study is to evaluate the real incidence of BTLs using routine posttransplant cholangiography as a more aggressive diagnosis approach for their detection.
Methods/Materials: From January 2000 to April 2009, 350 patients (median age: 55 years; range 16–70) underwent LT in our center. After excluding living donor LT ($n = 23$), perioperative deaths ($n = 25$), and patients refusing the protocol ($n = 47$), 255 patients surviving 3 months after LT were included in the study, including 249 who received donation after brain death graft and 6 donation after cardiac death graft. Duct-to-duct biliary anastomosis was performed in 225 patients, including 66 with T-tube, and 30 underwent a hepatico-jejunostomy. All cholangiographies were retrospectively reviewed and correlated with the evolution of the liver tests. Median follow-up was 126 months (4–194).
Results: Among the 255 patients, cholangiography was routinely performed at a median time of 5 months (1–7) either percutaneously or endoscopically. BTLs were diagnosed in 76 (30%) recipients, including 3 due to recurrent allograft disease (primary sclerosing cholangitis); 23 (9%) patients presented such BTL in the absence of liver test alterations or symptoms. Fifty-seven (75%) patients had anastomotic strictures, 12 (16%) non-anastomotic strictures and 7 (9%) presented both anastomotic and nonanastomotic strictures. Among patients without biliary stricture at routine cholangiography, 10 developed biliary stricture after a median time of 22 months (5–173) from LT; 3 of them were initially transplanted for primary sclerosing cholangitis.
Conclusion: Routine use of delayed cholangiography is a good diagnostic tool for detection of silent biliary stricture after LT, and may contribute to prevent complications of chronic cholestasis leading to secondary biliary cirrhosis.

BOS402 IMPLICATIONS OF DOPPLER ALTERATIONS ON OUTCOMES AFTER LIVER TRANSPLANTATION

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Backgrounds: Arterial thrombosis (HAT) is the most frequent vascular complication after liver transplantation, presenting in adults between 4–13%, and in children up to 26%. It is the 2nd most frequent cause of graft failure. Due to the important morbidity associated and the challenge that often involves diagnosis, the post-transplant Doppler studies are protocolized in the immediate follow-up of these patients. We aim to analyze the outcome of those patients with arterial doppler flow alterations without reaching criteria of thrombosis.
Methods: Between January 2009 and December 2015, 456 liver transplants were performed. 28 were pediatric patients. All of them underwent a Doppler in the first 24–48 hours. These alterations were mostly described as Resistance Index (RI) >0.8, although 2 cases with RI <0.5 have also been considered. Analysis were performed with 4 groups of adult patients: those with normal Doppler (A), altered Doppler without posterior complications (B), those who progressed to HAT (C) and those who only presented HAT (D).
Results: No differences have been found between groups with regard to MELD Score, DCD donors nor hemoderivatives transfusions.

Hepatocarcinoma (HC) was found with the following distribution: group A (43.47%), B (33.87%) and D (21.42%). None of patients in group C had HC ($p < 0.05$).

Doppler alterations were found in 111 cases, persisting in 39 cases. 8 of them presented progression to HAT. In the remaining 31, alteration persisted with no morbidity.

Of the 456 transplanted livers, 28 were pediatric patients. 11 presented alterations in Doppler, 3 of them progressing to HAT (27.27%). In the 428 adult transplants, 100 presented Doppler alterations, progressing 5% of HAT, whereas HAT in patients without previous Doppler abnormalities occurred in 6.54%.

We have found differences in patients and graft survival.
Conclusion: Doppler ultrasonography is an excellent tool for evaluating vascular complications, but altered values in RI do not always lead to complications.

Basic Pancreas/Islet Ischemia-Reperfusion and preservation

BOS403 DULAGLUTIDE PROTECTS β CELLS AGAINST CYTOKINE STRESS MIMICKING ISLET TRANSPLANTATION

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Background: Intra-portal islet transplantation is associated with IBMIR, an early inflammatory reaction with concomitant release of proinflammatory cytokines, procoagulant microparticles (MP), and by tissue factor (TF)-driven local coagulation, all favoring islets' cellular activation and damage. MP are plasma membrane vesicles and circulating biomarkers of cell stress and organ damage. In vitro, MPs shed from cytokine or oxidative stress-stimulated β cells act as cellular effectors prompting TF expression, cytokine release, apoptosis and reducing insulin secretion through GLP-1 receptor (GLP1R) dependent and independent pathways. We investigated whether Dulaglutide (Dula), a GLP-1 analog, could prevent cytokine-driven β cell dysfunction.
Methods/Materials: Rin-m5F Rat β cells were submitted for 24 hours to cytokines (cyt: 1000 IU/ml TNF-α, 50 IU/ml IL1β 1000 IU/ml INF-γ) in the presence of Dula (0.05–1 μM). GLP1R-dependent effects were inhibited by 200 nM exendin 9–39 (Ex), a GLP1R antagonist. Apoptosis was measured by Propidium Iodide/Annexin 5 staining, MP release by prothrombinase assay, insulin secretion by ELISA. TF activity at β cell surface was measured by tannase assay.
Results: Dula prevented cytokine-induced apoptosis (Cyt: 17%, Cyt-1 μM Dula 8%, Cyt-0.05 μM Dula 14%, $p < 0.01$, $n = 4$) restored insulin secretion. Ex strongly reversed apoptosis prevention (Cyt: 17% Dula: 9% Ex: 14% $n = 4$), indicating GLP1R dependence. Dula limited the cytokine-induced MP release in a GLP1R-dependent manner (Cyt: 12.2 nM, cyt+ 1 μM Dula: 10.6 nM, cyt+ Dula Ex: 12.8 nM/ cells, $p < 0.01$, $n = 4$) and decreased TF activity, independently of GLP1R (Cyt: 211 ± 27 fM, cyt+Dula: 113 ± 5 fM, cyt+Dula Ex: 95 fmol TF/50'000 cells, $p < 0.05$). 1 μM Dula also prevented apoptosis in isolated islets (Cyt: 40%, Cyt+Dula 19%, $p < 0.001$).
Conclusion: Dula exerts β cell cytoprotection by targeting GLP1R dependent and non-dependent pathways involving MP release and inflammatory responses. The interest

Clinical Pancreas/Islet Immunosuppressive agents

BOS404 COMPARISON OF ALEMTUZUMAB VS. BASILIXIMAB BASED IMMUNOSUPPRESSION REGIMES: LONG TERM OUTCOMES FOR SIMULTANEOUS PANCREAS AND KIDNEY (SPK) TRANSPLANTATION

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Introduction: Alemtuzumab is (anti CD52 antibody) a potent lymphocyte depleting induction agent that allows early reduction of Calcineurin Inhibitors (CNI) and steroid avoidance, making it particularly favourable for SPK transplants. We introduced Alemtuzumab for all our SPK recipients from March 2008 onwards along with a steroid-free maintenance regime of Tacrolimus and MMF. Prior to this, we used Basiliximab for induction with triple maintenance immunosuppression with steroids. We aimed to compare the 2 different regimes and assess long term outcomes.
Methods: A retrospective analysis of all our SPK transplant patients from January 2003 till December 2015. Information was gathered using electronic records and patient notes. Data was analysed using Microsoft Excel 2011 and SPSS 23. Kaplan-Meier analysis was used to assess patient and graft survival.
Results: A total of 79 SPK transplants were performed with either Alemtuzumab ($n = 49$) or Basiliximab ($n = 30$). There was no statistical difference in overall patient survival and graft survivals. Kaplan-Meier survival probability estimates are tabulated as below.

7 patients (14.2%) in the alemtuzumab group developed CMV infection at mean of 7.7 months (range 1.5–11 months) since transplantation. 3 patients (10%) in the basiliximab group developed CMV infection (at 6 months, 11 months, 5 years) post-transplant (p = ns).

Survival (%)	Year 1	Year 3	Year 5
Patient			
Alemtuzumab	96	93	90
Basiliximab	90	90	90
Kidney graft			
Alemtuzumab	90	85	85
Basiliximab	100	97	97
Pancreas graft			
Alemtuzumab	82	74	71
Basiliximab	87	83	69

Kaplan-Meier Survival Probability Estimates for Patient survival, Kidney and Pancreas Graft survival.
Conclusion: Despite a longer follow up period, patients receiving Basiliximab induction appear to have comparable rates of patient and graft survival. There appeared to be an increasing trend for kidney graft survival in the Basiliximab group. No differences in CMV infection rates were noted.

Clinical Pancreas/Islet Metabolic complications

BOS405 THE CKD-EPI EQUATION FAILS TO ESTIMATE GLOMERULAR FILTRATION RATE IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT RECIPIENTS

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Background: Estimating glomerular filtration rate (GFR) is of utmost importance for clinical management and research studies in simultaneous pancreas-kidney transplantation (SPK) recipients. No study has specifically investigated

the reliability of recent creatinine–based GFR estimating equations in this singular population. As a result, there is no specific recommendation and GFR is habitually estimated with the CKD-EPI or MDRD equation. Here, we compared the performances of the CKD-EPI, MDRD and Schwartz equations for estimating GFR one year after SPK.
Methods/Materials: Included were all adults who received a SPK between 2009 and 2015 and had a measurement of GFR one year after transplantation ($n = 126$). All plasma creatinine values were obtained by an enzymatic method traceable to the National Institute of Standards and Technology.
Results: In the whole population, mean absolute bias was 19.4 [15.4; 21.8] ml/min/1.73 m2 and mean 30% accuracy was 41.0 [34.0; 50.0] % with the CKD-EPI equation. Schwartz and MDRD equations were significantly less biased (8.65 [7.0; 11.0] and 11.5 [8.5; 13.5] ml/min/1.73 m^2, respectively, $p < 0.01$) and more accurate (74.0 [66.0; 81.5] and 65 [57.0; 73.5] %, respectively, $p < 0.01$). Conclusions were similar whatever the age class (< 40 or ≥ 40 yo) and mGFR level (< 60 or ≥ 60 ml/min/1.73 m^2).
Conclusion: We conclude that the CKD-EPI equation has insufficient performances and should not be used in SPK recipients. Schwartz or MDRD formulas have to be preferred.

Basic Pancreas/Islet Ischemia-Reperfusion and preservation

BOS406 DMSO-FREE CRYOPRESERVATION OF PANCREATIC ISLETS USING TREHALOSE AND MEMBRANE-PERMEABILISING BIOPOLYMER PP-50

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Introduction: The potential of pancreatic islet transplantation is hampered considerably by the lack of an effective cryopreservation protocol. The commonly used cryoprotectant dimethyl sulphoxide (DMSO) provides poor protection and is toxic. To address this unmet need, we tested the efficacy of the disaccharide trehalose with biopolymer PP-50 (backbone of poly(L-lysine isophthalamide) grafted with L-phenylalanine) to facilitate intracellular uptake of trehalose.
Methods: Isolated mouse pancreatic islets were cryopreserved with DMSO, trehalose alone or trehalose+PP-50 using a programmable freezer to achieve optimal freezing rate. The thawing procedure was optimised to keep the fragile islets intact and viable. After thawing, number of recovered islets was determined and islets were stained for viability with fluorescein diacetate/propidium iodide.
Results: As anticipated, cryopreservation with DMSO resulted in viability of only 56.5 ± 17.1%, reducing to 28.4 ± 11.6% after 3 days in culture. Trehalose alone did not provide sufficient protection to preserve any intact islets. The addition of PP-50 resulted in preservation of a comparable number of intact islets to DMSO (80.28% and 74.67% of the pre-freeze number, respectively) but very low viability. This loss of viability was evidently not a consequence of PP-50 toxicity since viability of fresh islets was maintained for up to 48 hours in culture with the polymer.
Conclusion: Our data suggest that the PP-50 polymer is non-toxic but its use in DMSO-free cryopreservation requires further optimisation. We therefore plan to investigate the efficacy of PP-50 and other polymer variants in increasing intracellular uptake of trehalose by islet cells using fluorescent labelling and trehalose quantification methods. Finally, we aim to replicate this work and optimize the protocol for human pancreatic islets.

Clinical Pancreas/Islet Other

BOS407 LIFE-STYLE (LF) AND QUALITY OF LIFE (QOL) IN TYPE 1 DIABETIC SUBJECTS (T1D) WITH FUNCTIONING OR FAILED PANCREAS TRANSPLANT ALONE (PTA)

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Background: little information is available regarding LS and QoL in T1D who have received a PTA.
Methods: in this study, previously validated questionnaires were administered to 37 recipients of a PTA (25 with insulin independence, InsInd, and 12 with graft failure, GF), whose main pertinent data are reported in the table.

	Ins Ind	GF
N	25	12
Age (years)	50 ± 9	46 ± 7
Gender (M/F)	10/15	7/5
BMI (kg/m^2)	23.4 ± 3.4	23.9 ± 3.3

Results: The InsInd group had an insulin independence duration of 10 ± 4 years; the GF group had lost pancreas function after 1.7 ± 2.3 yrs from transplant. Adherence to an healthy nutrition behavior (mediterranean diet) was better ($p < 0.05$) in the GF group, mainly due to higher intake of fruit, pulses and fish. Physical activity, as assessed by the IPAQ_SHORT questionnaire, was similar in the two groups. According to the SF-12 questionnaire, significantly more subjects in the InsInd group reported better ($p < 0.05$ or less) psychological well-being and improved physical performances.
Conclusion: These preliminary results suggest that a more regular assessment of LF and QoL in PTA subjects could allow better understanding of how to improve the health status in these individuals.

Clinical Pancreas/Islet Immunosuppressive agents

BOS408 LONG-TERM RESULTS FOLLOWING ALEMTUZUMAB VERSUS ATG INDUCTION THERAPY IN COMBINED KIDNEY-PANCREAS TRANSPLANTATION: A SINGLE CENTER REPORT

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Background: A retrospective long term analysis of patient, pancreatic/kidney graft survival and function, major complications comparing an induction therapy with Alemtuzumab to Antithymocyte globulin (ATG).
Methods/Materials: Totally 14 simultaneous kidney pancreas (SPK) transplants randomized to Alemtuzumab + Tacrolimus-monotherapy (group A, $n = 14$) and 16 SPK randomized to ATG + Tacrolimus + MMF + Steroids (group B, $n = 16$) performed at our center between 2006 and 2010 were retrospectively analyzed within a mean follow up period of 9.5 years post transplant.
Results: The 9 years survival (%) in group A/B concerning patients was 92.9/86.7, pancreas 75.0/65.0, kidney 83.1/93.8, respectively. In the surviving grafts the mean longterm values (mg/dl) in group A/B were: creatinine 2.1/1.3, fastening blood glucose 86.4/70.2; HbA1c 5.7/6.0 g%, lymphocytes absolute 1.7/1.5 G/l. Causes of death were tumor/sepsis in group A, cerebrovascular accident/unknown reason in group B. All other major complications were resolved: severe peripheral angiopathy (group A/B: 6/1), cerebrovascular ischaemia (group A:2), coronary revascularization (group A/B:2/1), hemolytic anemia (group A:1), partial portal vein thrombosis (group B:1). One lung cancer (fatal) occurred in group A, one B-cell-lymphoma/prostate cancer/cervix cancer each in group B. Apart from one fatal sepsis in group A all serious infections were reversible: one case each of pneumonia/bacteraemia/tuberculosis/recurrent cystitis in group A, osteomyelitis/BK-nephropathy/recurrent condylomata/hepatitis B in group B.
Conclusion: Good long term results in pancreatic / kidney graft survival were achieved in both groups. The long term graft function, patient survival, incidence of severe infectious complications were comparable. More serious vascular complications observed in group A might be explained by the individual grade of underlying angiopathy. More tumors occurred in group B, all survived, in contrast to one fatal malignancy group A.

Clinical Pancreas/Islet Rejection

BOS409 PREGNANCY OUTCOMES IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANT RECIPIENTS: A NATIONAL FRENCH SURVEY STUDY

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Background: Simultaneous pancreas and kidney transplantation (SPK) is currently the best therapeutic option for patients with type-1 diabetes and terminal renal failure. Renal transplantation restores fertility enabling women to pursue pregnancies. However, scarcity of available data on pregnancy outcomes in SPK impedes fair medical counseling.
Methods: Medical files of all pregnancies that lasted ≥3 months between 1993 and 2015 among recipients of successful SPK were retrospectively analyzed in France.

Renal and pancreas graft survivals were compared between women recipient of a SPK with and without pregnancy.
Results: Twenty-six pregnancies in 22 SPK recipients were identified. Main maternal complications included gestational hypertension (53.8%) and infections (50%). Caesarean section was performed in 73% of cases. Overall fetal survival was 92.6% with a mean gestational age of 34.2 ± 3 weeks. Four children (16.7% of live births) had a birth weight <10th percentile. Endocrine pancreas graft function remained stable during pregnancy. An acute kidney rejection occurred in 2 patients, one of which resulting in graft loss. Kidney and pancreas graft survival was respectively 96% and 100% at 1 year post-conception and did not differ from controls (Log Rank p value = 0.94 and 0.61 respectively).
Conclusion: Pregnancy in SPK is feasible, but patients should be informed of the risks for the fetus, the mother and the grafts. Planning of pregnancy in SPK women is key to allow a personalized multidisciplinary monitoring, which represents the most straightforward approach to optimize outcomes.

Basic Pancreas/Islet Other

BOS410 CO-CULTURE OF WHARTON'S JELLY-DERIVED MESENCHYMAL STEM CELLS WITH HUMAN PANCREATIC ISLETS FOR USING IN ISLET TRANSPLANTATION

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Islet transplantation is an alternative treatment to daily insulin injections for patients with type 1 diabetes. The keeping of viable pancreatic islets is crucial for successful islet transplantation. In order to overcome islet quality loss during culture, it has been proposed to co-culture pancreatic islets with Mesenchymal Stem Cells.

In this study, human pancreas islets were isolated according to enzymatic and mechanical protocol. Then purified islets were co-cultured with Wharton's jelly-derived mesenchymal stem cells. The expression of CD90, CD44, CD105, and CD34 and as well as osteogenic and adipogenic differentiation of mesenchymal stem cells were identified. Also, the islets were evaluated with DTZ staining and the amount of insulin released was assessed by ELISA assay.

The pancreatic Islets were viable and showed positive DTZ staining before co-culture. Wharton's jelly-derived mesenchymal stem cells expressed high levels of CD44, CD90, and partly CD105 as mesenchymal stem cells markers. However, these cells did not express hematopoietic marker CD34. The culture of islets alone resulted in cells death and loss of function after a few days. While, viability and functionality of co-cultured Wharton's jelly-derived mesenchymal stem cells with islets was higher than that of islets after 7 days.

Co-culture of islets with Wharton's jelly-derived mesenchymal stem cells has the potential for protecting islets from injury during culture period. Accordingly, by adjuvant co-transplantation of mesenchymal stem cells, the probability of successful outcomes of islet transplantation will increase.

Clinical Pancreas/Islet Surgical technique

BOS411 ENTERIC DRAINAGE OF PANCREAS TRANSPLANTATION: CLINICAL IMPACT OF INTRA-ABDOMINAL COMPLICATIONS

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Background: The aim of this study was to analyze retrospectively the surgical complications associated with enteric drainage in a single center over a period of 15 years.
Methods: From 2000 to 2015, 333 pancreas transplants were performed (SPK: 272, PAK: 23, PA: 3, Retransplantation: 35). Venous systemic vascular drainage was performed with porto-cava anastomosis. Arterial supply for the pancreatic graft was performed through the anastomosis of the right iliac primitive artery of the recipient with (i) the superior mesenteric artery of the graft or (ii) the common iliac graft artery. For exocrine secretion, enteric drainage was performed by side-to-side duodeno-jejunostomy anastomosis.
Results: Nineteen patients (5.7%) were identified with intestinal complications: intestinal obstruction in 7 patients, paralytic ileus in 4 patients, ischemic graft duodenum in 2 patient, dehiscence of duodeno-jejunostomy in 2 patients, intestinal fistula without anastomotic dehiscence in 3 patients and anastomotic dehiscence in jejunum after transplantectomy in one case of retransplantation. According Clavien-Dindo, complications were: Grade I: 10.5%, Grade II: 10.5%, Grade IIIb: 57.9% and Grade IVa: 21.1%. Fifteen patients required reoperation (lysis adhesions (n = 7), pancreas transplantectomy (n = 5), primary closure and intestinal bypass (n = 1), simple suture (n = 1), intestinal resection and anastomosis (n = 1). Vascular thrombosis diagnosed by imaging assessment was related with ischemic process of enteric drainage on 15.8% of cases (n = 3), with a significant correlation for graft loss in two of the cases.
Conclusions: Enteric drainage for exocrine secretion of graft pancreas is a safe and feasible technique with a low rate of complications. Vascular thrombosis associated with intestinal complications is a risk factor for the viability of pancreatic graft, so early detection is important.

BOS412 DUODENAL GRAFT COMPLICATIONS REQUIRING DUODENECTOMY AFTER PANCREAS AND PANCREAS-KIDNEY TRANSPLANTATION

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Background: Duodenal graft complications (DGC) are poorly reported complications of pancreas transplantation (PTx) that can lead to graft loss.
Methods/Materials: Pancreas grafts were procured, prepared at the back table (Surgery 2004, 135:629–41) and transplanted (Transplantation 2005, 79:1137–42) according to previously described techniques. As specifically regards blood supply to graft duodenum, the patency of collateral circulation between the superior mesenteric and splenic pedicles, was checked by injecting a small amount of preservation fluid into either the superior mesenteric artery or the splenic artery and observing outflow from opposite vascular pedicles.

After PTx, recipients were seen at our center every month during the first year, every three months during the second year, and every six months thereafter, if not otherwise necessary.

Once a DGC was suspected, contrast-enhanced computed tomography was performed to confirm diagnosis and define anatomy of the lesion. Complete immunologic and virologic work-ups were also performed in every patient.
Results: After a median follow-up period of 120 months (range 10–185) duodenectomy was required in 14 of 298 PTx recipients (4.3%). All recipients were insulin independent at the time of diagnosis. Reasons for duodenectomy were delayed duodenal graft perforation (n = 10, 71.5%), and refractory duodenal graft bleeding (n = 4, 28.5%).

In all patients with duodenal graft bleeding, the entire duodenum was removed. In patients with duodenal graft perforation preservation of a duodenal segment was possible in 5 patients. Completion duodenectomy was necessary in one patient. After total duodenectomy immediate enteric duct drainage was feasible in 7 patients. In 2 patients a pancreatico-cutaneous fistula was created, and was subsequently converted to enteric drainage in one patient. Spontaneous duct drainage into the ascending colon occurred in the other patient, without consequences and with sustained long-term graft func.

Translational Pancreas/Islet Donation and donor types

BOS413 AMIR-375 AND ELECTROPORATION METHOD FOR PRODUCING ISLET LIKE CELL CLUSTERS←

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Expression at the post-transcriptional level. MiRNAs have been shown to affect insulin levels by regulating insulin production, insulin exocytosis, and endocrine pancreas development. Based on some studies on miRNAs pattern, in this study investigated the Islet like cell clusters differentiation of human pluripotent mesenchymal stromal cells (PDB-MSCs) in adult placenta by up-regulation of miR-375 by electroporation method.

Human placental decidua basalis (PDB-MSCs) cells were cultivated from full term human placenta. The immunophenotype of isolated cells was checked for CD90, CD105, CD44, CD133 and CD34 markers. The PDB-MSCs (P3) was physically transfected with miR-375. The qRT-PCR results revealed the expressions of PDX1, KIR6.2, NKX6.1, PAX4, NGN3, GLUT2, insulin, Glucagon and OCT4 genes on the first and second days after physical transfection. On the second 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 first day, and cell clusters were formed on second day. Islet like cell clusters showed a deep red color with Dithizone. The expression of pancreatic specific transcription factors were increased on the first day and they had significantly increased on the second 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.

miR-375 and transcription factor network are important in pancreatic endocrine differentiation. Physical transfection with miR-375 can differentiate human PDB-MSCs cells into functional ILCs in a short time

Keywords: Diabetes, Pancreas, beta-cell, PDB-MSCs, miR-375

Clinical Pancreas/Islet Other

BOS414 LATE REPETITIVE BLEEDINGS FROM DUODENOJEJUNOSTOMY AFTER PANCREAS TRANSPLANTATION

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Objective: Enteric drainage has become the preferred surgical technique in pancreas transplantation. Since we have observed a number of late, repetitive bleedings from the site of the enteric anastomosis, we herein analyze the clinical courses.

Patients and methods: We retrospectively analysed all 379 pancreas transplantations consecutively performed between January 2000 and December 2016. Enteric anastomosis was performed in the upper jejunum as either hand sewn or machine stapled duodenojejunostomy. Bleeding was detected by decrease of serum haemoglobin and/or melena. Treatment consisted in endoscopic, angiographic intervention or surgery.

Results: 5 patients (0.013%) developed recurring late haemorrhagic episodes originating from the enteric pancreas anastomosis. The mean onset of bleeding episodes was 6.4 ± 2.8 (mean+SEM) years after transplantation. All five patients developed 5.2 ± 2.6 bleeding episodes requiring 9 ± 2.5 interventions. In total 20 enteroscopies, 12 gastroscopies, 9 colonoscopies and 3 angiographic interventions were needed to control the bleedings. Endoscopic assessment identified hypervascularization, vulnerability and bleedings at the site of the enteric anastomosis in all cases. Four patients were treated with resection of the enteric pancreas anastomosis and reconstruction with a novel duodenojejunostomy. No pancreas graft-loss occurred due to bleeding. In two patients, hepatic cirrhosis and portal hypertension was identified, one patient had a slight elevation in liver stiffness as putative cause for the repetitive bleedings. In the remaining two cases the cause remains unknown.

Conclusion: Late anastomotic haemorrhage is a rare but severe complication following pancreas transplantation. The treatment is challenging and includes endoscopy, interventional radiology and surgery. Hepatic conditions with an increase portal pressure may be the underlying cause.

BOS415 OVER IMMUNOSUPPRESSION IS A RISK FACTOR OF GVHD IN PANCREAS TRANSPLANT

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Background: raft-versus-Host Disease (GVHD) is a common complication after bone marrow transplantation but is rare in solid organs especially in pancreas transplant. Herein we reviewed reports on GVHD occurred in pancreas transplant including our recent case.

Method: ince 1986, there are 16 cases reported who developed GVHD after pancreas transplant through the MEDLINE. Those reports including our recent case were reviewed and analyzed.

Result: GVHD developed in 13 males and 3 female (2 reports did not describe sex). Average HLA mismatch was 3.2 (4 cases were not shown) but there were 2 cases with 0 mismatch. Nine cases were first transplant and 8 cases were more than 2nd transplant. Nine cases underwent SPK, 6 cases did PAK, and 2 did PTA. Timing of initial symptom was 21 days in median (7 days – 16 months). Initial symptoms were fever 10, diarrhea 4, and skin rash 3. Methods of definitive diagnosis were biopsy, short tandem repeat, FISH staining, and HLA typing. Only 5 cases (29.4%) survived with increase of immunosuppression.

Conclusion: GVHD after pancreas transplant is rare but does occur and fatal. GVHD seems to be developed in patients with strong immunosuppressive status (PAK, multiple transplant, post rejection therapy). Recipient with one-way crossmatch should be very carefully monitored. Early diagnosis and increase of immunosuppression targeting T-cell as well as protection of infectious complication are inevitable to save patients from fatal GVHD.

Clinical Kidney Donation and donor types

BOS416 DONOR AND RECIPIENT AGE DIFFERENCE IMPACT IN SURVIVAL OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Introduction: Age matching has largely been studied in single kidney transplant. Its association with patients' and grafts' survival in simultaneous kidney and pancreas transplant (SPKT) is not so clear.

Methods: We conducted a retrospective analysis on SPKT at our center from January 2000 to December 2016 ($n = 198$). Demographic and clinical characteristics of donors and recipients were collected. A preliminary evaluation of age difference between recipients and donors compared patients alive and those who died at the end of follow-up. The median age difference [Interquartile range] was (8 [−2.16] vs. 19 [0.25] years (y), p value=0.22) in each group, the last one being used as the cut-off, categorizing two groups: recipient less than 19y older or younger than donor (A, $n = 152$) or recipient more than 19y older than donor (B, $n = 46$).

Results: Patients median age was 35.0 ± 6.1 years-old, 50% women. Median follow-up time was 6.9 (3.7, 10.6) years. Recipients in group A were

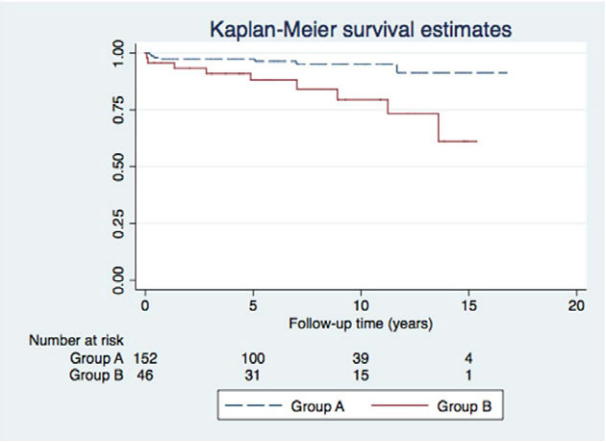

Figure 1. Kaplan-Meier patient's survival curves in Groups A and B.

significantly younger (34.0 ± 5.9 vs. 38.4 ± 5.3y, p < 0.001) and donors were older (31.3 ± 9.6 vs. 16.3 ± 4.0y, p < 0.001). Mean time on dialysis, dialysis modality, HTA prevalence, HbA1c level, smoking status, median hospitalization time and postoperative complications weren't significantly different between the two groups. Pancreas graft survival (78.3% vs. 82.6%, HR 1.1, 95% CI 0.5–2.6, p = 0.85) and kidney graft survival (89.5% vs. 87.0%, HR=1.0, 95% CI 0.7–5.5, p = 0.18) weren't significantly different between groups A and B, respectively. Even after adjusting for recipient's age, a difference of more than 19y from donor's age remained significantly associated with worst survival (HR 4.1, 95% CI 1.4–11.6, p = 0.009).
Conclusion: Recipients nearly 20y older than donors seem to have worse prognosis, although not directly dependent of kidney or pancreas graft survival.

Clinical Liver Cancer

BOS417 RETROSPECTIVE ANALYSIS OF THE CURRENT SITUATION OF LIVER TRANSPLANTATION FOR HCC IN GERMANY WITH SPECIAL REGARD TO PRE- AND POSTTRANSPLANT TUMOR STAGING

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Background: In selected patients liver transplantation (LTX) remains the best curative treatment for HCC in cirrhosis. In most countries, due to existing organ shortage, only patients with low tumor load fulfilling the Milan criteria are prioritized for LTX. However, classification of patients is based on pretransplant imaging diagnostics, bearing the risk of incorrect diagnosis.
Methods: We performed a retrospective multicenter analysis in all German LTX centers including all primary LTX for HCC (2007–2013). Data were collected based on Eurotransplant data base and surveys sent to German LTX centers.
Results: 1168 primary LTX for HCC were performed (age 57.9 ± 8.4 year, 78% male, 52% viral hepatitis). Tumor characteristics were pT1/2/3/4 39/45/16/1%, V1 21%, G1/2/3 17/73/11%. Outcome analysis revealed a significant better patient and recurrence free survival with low primary tumor staging, absent vascular invasion and higher differentiated tumor. Patients inside the Milan, UCSF and up-to-seven criteria based on imaging diagnostics (74%, 81%, 86%) or histology (66%, 77%, 81%) showed a superior outcome, irrespective of applied classification. Patients pretransplant outside the Milan, UCSF and up-to-seven criteria were misclassified in 34%, 43%, 41% and patients inside the criteria were misclassified in 18%, 15%, 11% when looking at histology. 22% of the patients suffered from HCC recurrence mean 1.9 ± 1.5 year after LTX. In these patients misclassification inside the criteria was remarkable higher (42%, 31%, 22%).
Conclusion: We found a good outcome correlation with tumor staging, grading and the Milan, UCSF and up-to-seven criteria based on histology. In contrast, there was a relevant misclassification (10–40%) by imaging diagnostics possibly resulting in exclusion of patients or non-indicated transplantations. Likewise, there was a reduced correlation between stage, based on imaging diagnostics, and outcome, suggesting the need for an adjustment of the HCC selection and allocation criteria.

BOS418 MIXED HCC-CHOLANGIOCARCINOMA AND INTRAHEPATIC CHOLANGIOCARCINOMA IN PATIENTS UNDERGOING LIVER TRANSPLANTATION FOR HCC

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Background: The incidence of mixed hepatocellular carcinoma-cholangiocarcinoma (HCC-CC) and intrahepatic cholangiocarcinoma (ICC) is increasing among patients with cirrhosis. The aim of this study was to evaluate the incidence, imaging features, and post-transplant outcomes for patients who underwent liver transplantation (LT) for HCC and were found to have HCC-CC or ICC in the explant.
Methods/Materials: We retrospectively reviewed the clinicopathological records of 243 adult patients who underwent LT for HCC between September 2004 and June 2016.
Results: In the explant specimens of 15 patients (6.1%), mixed HCC-CC (n = 10) or ICC (n = 5) was identified. This HCC-CC/ICC group had significantly higher carbohydrate antigen (CA 19–9) (704 ± 1125 ng/ml vs. 48.7 ± 55.2 ng/ml, p < 0.001) and significantly lower alpha-fetoprotein (AFP) levels than those with pure HCC. In a median follow-up period of 14 (IQR, 8–32) months, 11 of 15 patients (73.3%) were found with tumor recurrence within a median time of 5 (IQR, 3–8) months. The HCC-CC/ICC group had a significantly higher incidence of FDG positivity with a significantly higher SUVmax values (5.8 ± 2.8 vs. 3.0 ± 2.3, p = 0.008) in the pre-transplant PET-CT evaluation (25.9% vs. 85.7%, p = 0.003). Both 5-year disease free survival (24.0% vs. 78.5%, p < 0.001) and overall survival rates (26.6% vs. 65.2%, p = 0.004) were significantly lower in the HCC-CC/ICC group. In the retrospective review of pre-transplant dynamic contrast-enhanced imaging, 9 of 15 patients showed imaging features that were suspicious for HCC.
Conclusion: Mixed HCC-CC and ICC are associated with a high rate of tumor recurrence and a poor prognosis after LT. Given the fact that both tumors exhibit radiologic and PET-CT features that are distinct from those observed with HCC, patients with HCC-CC/ICC should be identified and excluded during the pre-transplant evaluation.

BOS419 LIVING-DONOR LIVER TRANSPLANTATION (LDLT), AN INNOVATIVE APPROACH IN THE TREATMENT OF NON-RESECTABLE SECONDARY LIVER TUMOURS: A RETROSPECTIVE STUDY COMPARING POST-MORTEM LT AND LDLT

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Background: Recent experiences have shown that patients presenting with non-resectable secondary tumours may benefit from liver transplantation (LT). However, this indication has fuelled ethical debates about the justification to allocate scarce organs to patients presenting a wide variation in outcome. Living-donor LT (LDLT) may represent an effective means to answer this question.
Methods and materials: We retrospectively analysed 24 patients [5 (21%) women and 19 (79%) men] transplanted during the period 1984–2016 because of non-resectable neuroendocrine (20–83%) and colorectal liver metastases (4–17%). Their median age was 52 years (IQR 43–55). Thirteen (54%) patients underwent post-mortem LT (PMLT) and 11 (46%) LDLT. PMLT consisted of 12 (92%) full-size and 1 (8%) split LT; LDLT of 4 (36%) right (segments V-VIII) and 7 (63%) left (segments I–IV) liver grafts. Median graft-to-body-weight ratios in the two groups were 1.03 (range 0.86–1.3) and 0.59 (range 0.51–0.91) respectively. Median follow-up for the PMLT and LDLT was 46 (IQR 17–68) and 11 (IQR 6–87) months.
Results: One- and 5-year overall patient survival rates were 77 and 44% for PMLT and 100% for LDLT (Log Rank p = 0.01). One- and five-year graft survival rates were 69 and 31% for PMLT and 88 for LDLT (Log Rank p = 0.01). Considering only death-censored graft survival and, notably, recurrence-free survival, no statistically significant differences were observed between groups. One living donor presented a Clavien-Dindo IVA complication but no deaths were registered.
Conclusions: This small single centre study shows that LDLT compared favourably to PMLT in the treatment of non-resectable liver secondaries. LDLT may become a promising add to therapeutic armamentarium for well-selected patients harbouring non-resectable secondary liver malignancies. Moreover LDLT has the advantage to not interfere with the limited PM allograft pool and to allow thereby to further progress in this critical field of transplant oncology.

BOS420 DIAGNOSTIC PREDICTABILITY OF BLOOD TUMOR MARKERS FOR HEPATOCELLULAR CARCINOMA IN PATIENTS WITH LIVER CIRRHOSIS UNDERGOING LIVER TRANSPLANTATION

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Background: This study was aimed to investigate the diagnostic role of alpha-fetoprotein (AFP) and DCP (des-gamma-carboxy prothrombin) for hepatocellular carcinoma (HCC) in patients with advanced liver cirrhosis waiting for liver transplantation (LT).
Material/Methods: During a study period of 10 years, 2074 adult LT recipients were identified. They were divided into two groups as HCC (n = 970; 46.8%) and non-HCC (n = 1104; 53.2%) groups. They were stratified into 5 categories as model for end-stage liver disease (MELD) score <10 (category A: n = 464), ≥10 and <15 (category B: n = 632), ≥15 and <20 (category C: n = 355), ≥20 and <30 (category D: n = 340), and ≥30 (category E: n = 283).
Results: Median pretransplant AFP vs. DCP levels were 11.3 ng/ml vs. 26 mAU/ml and 4.2 ng/ml vs. 22 mAU/ml in the HCC and non-HCC groups, respectively. Receiver operating characteristic curve analysis showed that area under the curve (AUC) of AFP was 0.693 having a cutoff at 6.8 ng/ml with sensitivity of 64.5% and specificity of 64.5%. AUC of AFP was inversely correlated with MELD score. AUC of DCP was 0.546 having a cutoff at 25 mAU/ml with sensitivity of 53.1% and specificity of 51.8%. AUC of DCP was lower than 0.6 except in category E.
Conclusions: Diagnostic predictability of AFP was reliably associated with MELD score, but that of DCP was not. The sensitivity of AFP and DCP is not high enough especially in patients with MELD score ≥20, thus thorough HCC screening with imaging studies should be performed during the waiting period for LT and pretransplant assessment.

BOS421 ALLELIC IMBALANCE ANALYSIS FOR HCC RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) due to hepatocellular carcinoma (HCC), despite the careful selection of patients, remains a controversial issue, because the current staging systems are not sufficiently predictive of the risk of post-transplant cancer recurrence (HCCr). We aimed to analyze the allelic imbalance (or loss of heterozygosity – LOH) in specific microsatellites and to assess the risk of HCCr in a consecutive series of patients with HCC underwent to LT in a single center.
Methods/Materials: Seventeen-one patients underwent to liver transplantation for HCC at ISMETT were included in this retrospective study, 18 of them developed HCCr at 5-years post-LT. Molecular analysis, using 19 microsatellites, was performed on whole blood and on corresponding native liver with HCC. The presence of allelic imbalance for a specific locus (*LOH*) was determined for values outside the normal range (0.66–1.50). The 19 microsatellites were subsequently divided into *panels*. to evaluate fractional allelic imbalance (FAI) cut-point index with the ROC analysis.
Results: We found a significant association between allelic imbalance and HCCr only in 3 loci (D3S2303, D9S251, and D9S254). We found a significant association with HCCr only in the two *panels* including the 9 microsatellites: the FAI index correctly classifies on average 74% of patients. We noticed that FAI index predicts HCCr within 2 years from transplant on average 69% of patients confirming the high predictive role of allelic imbalance in D9S251, especially in early HCC recurrence.
Conclusions: We detected a panel of microsatellites that could identify, with sufficient specificity and sensitivity, a subgroup of patients with a high risk of post-transplant HCC recurrence in our study population.

BOS422 A PROSPECTIVE STUDY TO EVALUATE THE IMPACT OF EARLY EVEROLIMUS ON THE RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: Everolimus (EVE) is prescribed to prevent hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) in absence of supporting clinical evidence. We aimed to evaluate the impact of early initiated EVE on the recurrence of HCC after LT.
Methods: Prospective study including a consecutive cohort of patients with HCC who underwent LT in two centers (2012–2015), and received a combination of reduced tacrolimus and early initiated EVE (15–21 days post-LT). A historical control group (ratio 2:1) matched by number and diameter of nodules, grade of differentiation and microvascular invasion (mVI), was used for analysis (none of them had received EVE). Post-LT follow-up ended in October 2016.
Results: 207 patients were included (88.4% male, mean age 55.6). Among them, 69 prospectively enrolled patients who received early EVE (cases) were compared with 138 matched historical controls. Cases and controls were comparable in terms of aetiology of liver disease, pre-LT AFP ($p = 0.98$), bridging locoregional therapy ($p = 0.20$), tumors beyond Milan criteria (23.5% vs. 27.5%; $p = 0.54$), and moderate-poor tumor differentiation (61.5% vs. 63.6%; $p = 0.80$). The rates of mVI were increased in cases as compared with controls (27.9% vs. 13.2%; $p = 0.01$). The use of EVE had no impact on HCC recurrence, neither in the overall cohort (12.8% in cases vs. 12.4% in controls at 36 months; $p = 0.89$), nor in subgroups with mVI ($p = 0.26$) or exceeding Milan criteria ($p = 0.23$). In the multiple Cox's regression analysis, the number of nodules and mVI status were predictors of HCC recurrence (RR = 1.01; $p = 0.025$ and RR = 5.47; $p < 0.001$), whereas the use of EVE was not (RR = 0.78; $p = 0.68$). Overall mortality rates were similar between cases and controls: 28.6% vs. 27.5% respectively at 36 months ($p = 0.74$).
Conclusions: Early initiated EVE does not prevent HCC recurrence after LT. Randomized trials focusing on high-risk subpopulations, particularly outside Milan criteria or with mVI, are warranted.

BOS423 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA AFTER DOWNSTAGING WITH YTTRIUM-90 RADIOEMBOLIZATION

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Background: Liver Transplantation (LT) is a well-established procedure for Hepatocellular Carcinoma (HCC) within the Milan criteria. Yttrium-90 microspheres radioembolization (Y90-RE) has shown to be an effective and safe treatment of primary liver tumors. We retrospectively evaluate the efficacy of the Y90-RE in patients with HCC prior to LT.
Methods: From January 2002 to December 2016, 390 patients were transplanted at the San Camillo Hospital Center. 162 patients were transplanted for HCC and in 25 cases the patients were treated with Y90-RE before LT.
Results: Three patients were treated with Y90-RE within the Milan criteria and 22 patients were out of criteria before Y90-RE. Four patients had an increasing MELD score between Y90-RE and LT. On the other hand alpha-fetoprotein decreased after Y90-RE treatment in all cases. No patient death was observed at Y90-RE procedure or at LT.

From Y90-RE treatment overall survival was 43.9 months. From LT, overall mean survival was 30.2 months with a free-survival of 29.6 months. The overall survival after LT analysis between the patients treated with Y90-RE and patients without was not significant ($p = 0.113$). Free survival analysis was not significant ($p = 0.897$) between the two populations.
Conclusions: We successfully performed LT in patients after Y90-RE treatment both as bridge and down-staging for HCC and obtain a similar overall and free survival of LT for HCC within Milan criteria. Y90-RE becomes a real option to provide curative therapy for patients who traditionally are not considered eligible for surgery.

BOS424 LONG-TERM OUTCOME OF LIVER RESECTION VS. TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN A REGION WHERE LIVING DONATION IS A MAIN SOURCE

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Background: The aim of this study is to define the best curative strategy in patients with hepatocellular carcinoma (HCC) in hepatitis B virus (HBV)-endemic region where living donation dominates cadaveric donation for liver transplantation (LT).
Material/Methods: We formed a retrospective cohort comprising those patients whose clinical course could potentially be traced for at least 10 years. From March 1997 to August 2006, 262 HCC patients underwent curative surgical treatment. Among them, 156 patients were treated with liver resection (LR) (R group), and 106 patients underwent LT (T group, 100 patients with living donor). Tumor characteristics, overall survival (OS), and recurrence-free survival (RFS) were analyzed.
Results: Postoperative mortality was not significantly different between the groups, whereas recurrence rate during the study period (until August 2016) was higher in the R group (56% vs. 19% in T group, $p < 0.001$). The 10- and 15-year OS and RFS were better in the T group. Subgroup analysis with patients having solitary and ≤5 cm tumors by preoperative imaging showed that the 10- and 15-year OS and RFS were much better in the T group, irrespective of their preoperative liver function defined by MELD score. In this group, resection as the surgical procedure and tumor size on histology were poor prognostic factors for RFS. Importantly, this superiority of LT over LR in OS and RFS applied only to the patients with relatively low preoperative alpha-fetoprotein (AFP) levels (AFP < 100 ng/ml), because patients with higher levels of AFP tended to have more recurrent tumors after LT, not LR, during long-term follow-up.
Conclusion: Overall, LT was associated with better survival outcomes than resection in patients with HCC in Korea, where living donation is a main source.

BOS425 RADIOFREQUENCY ABLATION (RFA) IS SO EFFECTIVE THAT IT SHOULD BE USED IN A SALVAGE RATHER THAN A BRIDGING STRATEGY FOR LIVER TRANSPLANTATION (LT)

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Background: Liver transplantation is the treatment of choice in HCC and liver failure and RFA has been established as a bridging treatment for selected patients on LT waiting lists. This study investigated the outcomes of patients with HCC treated with RFA either as a bridge to transplantation or as a primary treatment to control local disease in those not eligible for transplantation.
Methods: Patients with HCC undergoing RFA over a 6 year period in a single centre were included. Primary outcomes were local recurrence at the RFA site and disease free survival in the group on imaging. In transplant recipients the native hepatectomy histology was reviewed for evidence of active disease at the site of RFA.
Results: 111 patients (84 m:27 f) with 120 de novo HCCs underwent RFA, with a mean size of 19.5 mm (6–38 mm). Follow up varied from 7 to >76 months. Radiological recurrence at the site of the RFA was seen in 5.4%, at a median 463 (26–1054) days following RFA. Recurrence of HCC at remote sites was seen in 19 patients (17.1%). Death primarily caused by HCC or liver disease was seen in 10 patients and 1 patient died whilst awaiting LT, overall survival is shown in Fig. 1.

16 of 24 patients listed underwent OLT. Analysis of histology from explanted livers showed evidence of residual disease in 2 cases, one was 20 days post RFA and showed features of ablation with small areas of viable tumour, the other showed a small satellite nodule, invisible on radiological imaging.
Conclusion: Our data supports the use of RFA in HCC as both a treatment and bridge to transplantation. The low rate of local recurrence raises the possibility that patients undergoing RFA with good synthetic liver function should be regarded as having potentially curative treatment and be removed from LT waiting lists with a view to salvage transplantation for recurrent disease.

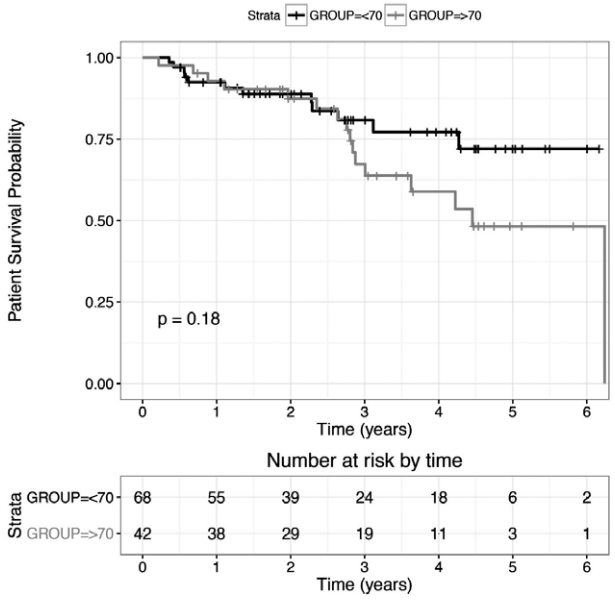

Fig. 1: Kaplan–Meier Curve of overall survival.

BOS426 PROGNOSTIC EFFECT OF COMPLETE PATHOLOGIC RESPONSE AFTER TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION FOR HEPATOCELLULAR CARCINOMA

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Transcatheter arterial chemoembolization (TACE)-induced complete pathological response (CPR) is known to improve post-resection outcomes of hepatocellular carcinoma (HCC). We aimed to assess the prognostic effects of CPR after preoperative TACE for HCC in patients who underwent hepatic resection (HR) or liver transplantation (LT). The clinical outcomes of patients showing CPR after HR ($n = 110$) or LT ($n = 233$) were analyzed. The control groups comprised patients with minimal recurrence risk as naïve single HCC ≤ 2 cm for HR ($n = 476$), and one or two HCCs ≤ 2 cm for LT ($n = 184$). Among HR study patients, 1-, 3-, and 5-year tumor recurrence rates were 18.5%, 50.6%, and 58.7% respectively, which were higher than those of controls ($p < 0.001$). The 1-, 3-, and 5-year patient survival rates were 97.8%, 82.0%, and 69.1% respectively, which were lower than those of controls ($p < 0.001$). Among LT study patients, 1-, 3-, and 5-year tumor recurrence rates were 4.1%, 7.9%, and 7.9% respectively, which were higher than those of controls ($p = 0.019$). The 1-, 3-, and 5-year patient survival rates were 92.7%, 89.2%, and 86.9% respectively, which were not different than those of controls ($p = 0.11$). LT recipients had lower recurrence and higher survival rates compared to HR patients ($p < 0.001$). Tumor recurrence site was mainly intrahepatic in HR patients. There was no difference between the incidences of extrahepatic recurrence in HR study group and all-site recurrence in LT study group ($p = 0.61$). We concluded that the prognostic effect of TACE-induced CPR for HCC patients appears to be limited to downstaging. LT recipients are benefited more from CPR than HR patients.

BOS427 THE IMPACT OF BIOLOGICAL MARKERS FOR THE SELECTION OF PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA FOR LIVING DONOR LIVER TRANSPLANTATION

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Recently, many extended criteria beyond the Milan criteria (MC) have been proposed in especially living donor liver transplantation (LDLT). The current morphology-based selection criteria was insufficient to the risk of tumor recurrence and so to explore optimal criteria beyond MC, biological markers are needed to achieve the maximal benefit of LT for HCC. The aim of this study was to evaluate the role of preoperative biological markers in selecting HCC patients beyond MC for LDLT.

A total of 67 LDLT recipients with HCC exceeding the MC between April 2007 and July 2016 were reviewed. Univariate and multivariate analyses with several preoperative variables focusing on the morphological parameters, Maximal standardized uptake value (SUVmax) of the tumor on (18)F-fluorodeoxyglucose positron emission tomography ((18)F-FDG PET), alpha-fetoprotein (AFP), protein induced by vitamin K absence or antagonist-II (PIVKA-II) were performed to find pre-transplant prognostic factors.

The cut-off values for serum alpha-fetoprotein (AFP) levels (370 ng/ml), protein induced by vitamin K absence or antagonist-II (PIVKA-II) levels (130 mAU/ml) and tumor maximal standardized uptake value (SUVmax) on (18)F-fluorodeoxyglucose positron emission tomography ((18)F-FDG PET) (4.24) were determined by c-statistics using receiver operating characteristic curves. Serum PIVKA II level (hazard ratio (HR) 3.596, 95% CI 1.466–8.823;

p = 0.005) and tumor SUVmax (HR 4.093, 95% CI 1.466–8.823; p = 0.005) were the only significant pre-transplant prognostic factors in the multivariate analysis. The low-risk group with PIVKA II ≤ 130 mAU/ml and SUVmax ≤ 4.24 had a significant lower 5-year recurrence rate than the other patients (p = 0.000) and had disease free survival rate comparable to that of the patients within MC (p > 0.05).

In conclusion, the combination of the serum PIVKA II level and tumor SUV max of (18)F-FDG PET could be considered as useful tools for expanding the selection criteria to LDLT for HCC.

BOS428 HEPATECTOMY VS. LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA WITHIN MILAN CRITERIA: ONE HOSPITAL EXPERIENCE IN SOUTH KOREA

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Introduction: We present the clinical result of hepatic resection (HR) and liver transplantation (LT) for patients with hepatocellular carcinoma (HCC) at Ajou University Medical Center, South Korea.
Method: We collected data of 312 patients with HCC within Milan criteria from Mar 2005 to Feb 2015, and divided into two groups for HR and LT based on their primary treatments. Survival curves and prognostic factors for survival were evaluated using the Kaplan–Meier method and Cox's regression test.
Result: For disease-free survival (DFS), HR group showed that 1-year DFS was 87.5%, 3-year DFS was 69.0%, and 5-year DFS was 59.5%. LT group showed that 1-year DFS was 94.5%, 3-year DFS was 93.0%, and 5-year DFS was 93.0%. (p < 0.05) HR group underwent multiple kinds of treatment after recurrence, and they were trans-hepatic arterial chemoembolization (TACE; 52%), radiofrequency ablation (RFA; 22%), surgical resection (11%), radiotherapy (9%), and salvage LT (6%). For overall survival (OS), HR group showed that 1-year OS was 97.5%, 3-year OS was 93.8%, and 5-year OS was 89.7%. LT group showed that 1-year OS was 92.2%, 3-year OS was 90.8%, and 5-year OS was 84.7% (n.s.).
Conclusion: We believe our findings support LT is superior to HR for HCC within Milan criteria from the perspective of DFS. We think we could perform many kinds of effective treatment option like TACE or LT after recurrence in HR group, and that it should be the reason why OS between the two groups was not statistically significant.

BOS429 RADIOFREQUENCY ABLATION AS THE FIRST TREATMENT OPTION FOR HCC IN TRANSPLANTABLE PATIENTS. IS THIS THE BEST STRATEGY?

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Background: Patients that are eligible for liver transplantation (LT) with small (≤3 cm) unifocal hepatocellular carcinoma (HCC) often receive radiofrequency ablation (RFA) as first-line treatment. Some will later recur outside criteria for transplantation. Our aim was to study LT-eligible patients with unifocal small HCC, determine rates of recurrence post-RFA, and risk factors for recurrence outside Milan criteria.
Methods: We retrospectively reviewed all transplantable patients who ever underwent RFA with curative intent at our centre for single HCC ≤ 3 cm. Exclusion criteria were: contraindications to LT at initial RFA, prior HCC treatment, failure to eradicate HCC on post-treatment contrast imaging, or transplant listing prior to first recurrence.
Results: Between 2000 and 2015, 328 patients met the study criteria. Mean age was 58 ± 7.7. Most were male (74%) and Child-Pugh A (86%). Recurrence occurred in the majority (64%). Progression outside Milan occurred in 81/328 (25%); 54/81 (67%) due to extrahepatic disease or vascular invasion and 27/81 (33%) due to tumor size/number. Thirty-seven (11%) were outside Milan at initial recurrence. Median time to recurrence outside Milan was 19 months. On univariate analysis, larger tumor diameter (p = 0.007), and poorly differentiated tumor pathology (p = 0.008) were associated with initial recurrence outside Milan. The association with tumor differentiation was maintained on multivariate logistic regression [HR 5.4 (95% CI 1.3–22.4); p = 0.02]. Patients with poorly-differentiated tumors had a 44% chance of initial recurrence outside Milan, compared to 13% of those with well- or moderately-differentiated tumors (p = 0.008).
Conclusions: RFA can be an effective treatment for small unifocal HCC in transplantable patients, though the proportion of recurrence outside Milan (25%) is concerning. Those with poorly differentiated or larger tumors are at risk of initial recurrence outside Milan, thereby losing the opportunity for salvage LT after recurrence.

BOS430 LIVER TRANSPLANTATION FOR COMBINED HEPATOCELLULAR CARCINOMA AND CHOLANGIOCARCINOMA A CASE MATCH ANALYSIS

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Background: Combined hepatocellular carcinoma and cholangiocarcinoma (cHCC–CC) is a rare tumor of difficult differential diagnosis with hepatocellular carcinoma (HCC) or cholangiocarcinoma (CC). Therefore some patients who undergo liver transplantation (LT) for a supposed HCC are eventually diagnosed with cHCC-CC.

The aims of this study is to evaluate incidence, characteristics, preoperative treatments and post transplant outcomes of patients who underwent LT for HCC and were found to have cHCC-CC at final pathology.
Materials and methods: Since 1991 to 2012 we retrospectively analyzed all patients who underwent LT for cHCC-CC in our Center. Pathologic specimens were re-analyzed to confirm the diagnosis. Demographics, clinical data, survival and outcomes after LT were compared to patients with HCC. Furthermore we performed a case match analysis pairing patients 1:2 (cHCC-CC: HCC) by age, sex, and the following pre-LT tumor characteristics: number of nodules, maximum size of biggest nodule and sum of total tumors diameter.
Results: During the study period 24 patients underwent LT for cHCC-CC and 299 for HCC. Patients affected by cHCC-CC were younger (55.9 vs. 60.3 years; p = 0.01). No differences were found in preoperative patient and tumor characteristics. Patients affected by HCC received significantly more pre-LT treatments (p = 0.03), particularly alcohol injection (p = 0.02). No differences in recurrence were found (cHCC-CC 22.2% vs. HCC 20.4%). Survival at 1 and 3 years were significantly different between groups (85% and 75% for HCC vs. 67% and 60% for cHCC-CC; p = 0.04). When cHCC-CC and HCC were paired with a ratio 1:2 no differences in overall survival were observed.
Conclusion: In our experience cHCC-CC and HCC had a similar recurrence rate and a similar oncologic outcome according to the case match analysis. Preoperative diagnosis of cHCC-CC is often not possible and no clinical protocols are described regarding best immunosuppression regimen or adjuv.

Clinical Liver Immunosuppressive agents

BOS431 IS POOR OUTCOME OF LIVING DONOR LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS THE NATURE OF THE DISEASE ITSELF OR INSUFFICIENT IMMUNOSUPPRESSION?

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Background: Indeed, liver transplantation (LT) is regarded as the only treatment of primary sclerosing cholangitis (PSC), but Japanese Liver Transplant Society reported that outcome of living donor LT (LDLT) for PSC is poorer than those of the other diseases. Recurrence of PSC and bile duct malignancies are supposed to be negative survival factors.
Methods: In consecutive 371 LTs from 1996 to 2015 (living 346, deceased 25), 12 cases of PSC recipients (living 11, deceased 1) were enrolled and analyzed in this retrospective study. Six recipients (50%) were accompanied by ulcerative colitis. Immunosuppression was composed of tacrolimus and steroid. Mycophenolate mofetil was added to aforementioned two drugs after 2002. Our unique protocol included 3 days half dose pulse (10 mg/kg, day 5 to 7) as the prophylactic diagnostic therapy against severe cellular rejection of PSC and persistent administration of oral steroid (>3 years).
Results: Out of 11 LDLT, 4 were lost by 2 cases of severe rejection (ABO incompatible antibody and accelerated acute rejection) and 2 cases of development of undiagnosable coexisting cholangiocarcinoma. There were 7 related pairs including 5 in parent-child relation and two siblings. Although one recipient out of 5 parent-child related pair was diagnosed as histological relapse 6 years after LT, he is doing well 7 years after identification of relapse without graft loss. On the other hand, histological relapse in only one case of deceased donor LT were diagnosed 4 years after LT. Certainly, three (75%) and 5 year-survival (64.3%) of PSC were lower than those of the other disease but none of the patient or graft was lost by relapse of PSC.
Conclusion: Intensive induction therapy including programmed pulse and persistent administration of steroid may prevent graft loss by relapse of PSC.

Surer diagnosis of co-existing cholangiocarcinoma and development of pretreatment for pre-sensitizing antibodies will improve outcome of LT, especially LDL.

BOS432 THE IMPACT OF CONVERSION FROM PROGRAF TO GENERIC TACROLIMUS IN LIVER TRANSPLANT RECIPIENTS WITH STABLE GRAFT FUNCTION

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Background: Bioequivalence, the safety and efficacy of the recently available generic Tacrolimus formulation (Adoport; Sandoz), to the reference product (Prograf; Astellas Pharma) in liver transplant (LT) patients have not been evaluated.
Methods/Materials: Tacrolimus trough concentrations and indices of liver function were recorded before and after generic substitution in 80 LT recipients and compared with case matched 80 LT recipients with the reference product. Inclusion criteria included age >18 years, LT recipient at least 6 months posttransplant, switched from the reference tacrolimus product to the generic formulation (Adoport; Sandoz) from January 2016 to September 2016, and on a stable dose of tacrolimus for at least 14 days prior to the switch. All subjects received care in the outpatient transplant clinic where tacrolimus trough concentrations, weight, total bilirubin, albumin, serum creatinine, alkaline phosphatase, ALT, AST, GGTP and graft rejection status was routinely monitored. Patients were followed for a minimum of 14 days and a maximum of 90 days before and after the generic conversion. At the time of the switch from the reference to generic product, a 1:1 dose conversion was employed and the dose of generic tacrolimus was then adjusted at the discretion of the treating physician to maintain trough concentrations within the therapeutic range.
Results: The tacrolimus concentration to dose (C/D) ratio was calculated for each trough concentration. In LT patients, the mean tacrolimus C/D ratio (±SD) was 178.1 (±123.2) ([ng/ml]/[mg/kg/day]) for the reference product and 150.7 (±87.8) ([ng/ml]/[mg/kg/day]) for the generic product ($p < 0.05$). No change was observed in biochemical indices of liver or kidney function and no cases of acute rejection occurred following the substitution.
Conclusions: LT patients currently taking the reference tacrolimus formulation may be safely switched to the Sandoz-generic product (Adoport) provided trough concentrations are closely monitored.

BOS433 RENAL PROTECTION STRATEGIES ARE POORLY IMPLEMENTED AFTER LIVER TRANSPLANTATION: THE 12-MONTH RESULTS OF THE ITALIAN NATIONAL STUDY SURF

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Background: No study has previously investigated the level of implementation of renal protection strategies after liver transplantation.
Materials and methods: SURF was a hybrid-design study in adult (≥18 years) recipients of a primary liver graft. Patients were enrolled 6 (±1) to 60 (±6) months after transplantation (phase 1, cross-sectional), and followed-up for 12 months (phase 2, longitudinal). The primary endpoints were: (i) to explore the prevalence of chronic kidney failure (CKD) defined as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2; (ii) the evolution of renal function from transplantation to inclusion visit (retrospective) and from inclusion to endpoint (prospective), and (iii) to investigate implementation of immunosuppressive adjustments for CKD. Concurrent with study initiation, a set of clinical recommendations on renal function management derived from the available literature was provided to all study investigators.
Results: A total of 738 patients were included in phase 2 (male 76%; median (IQR) age 57 (51; 63) years; Caucasian 99%). The prevalence of CKD increased from 16.7% at transplantation ($n = 110$), to 25.3% at inclusion ($n = 187$), to 27.9% at endpoint ($n = 206$). The median (IQR) eGFR decrease from transplantation to follow-up visit was: −20.6 (−41.0; −2.7) ml/min/1.73 m^2 ($p = <0.0001$) for MELD scores <15; −17.7 (−39.2; 2.2) ml/min/1.73 m^2 ($p = <0.0001$) for MELD scores 15–24; and −7.4 (−27.6; 17.9) ml/min/1.73 m^2 for MELD scores >24 ($p = 0.1096$). Out of the potentially eligible 187 patients, only 39 (19.2%) underwent any adjustment in their immunosuppressive schedule as recommended, and 6 (3.2%) experienced improvement in renal function (i.e. eGFR>60 ml/min/1.73 m^2).
Conclusions: Immunosuppressive modifications in view of improving renal function deterioration are poorly implemented in clinical practice. Further national initiatives to build awareness are highly needed.

BOS434 DONOR AGE PREDICTS TACROLIMUS INDUCED NEUROTOXICITY AFTER LIVER TRANSPLANTATION

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Background: Calcineurine inhibitors induced neurotoxicity (CIIN) is one of the most common, serious and debilitating side effects after liver transplantation (LT). Risk factors and impact on patient outcomes are not well defined. Our aim was to assess the incidence, risk factors associated and the clinical outcome of CIIN.
Methods: We retrospectively analyzed 175 LT in 160 recipients performed at our centre between January of 2010 and September of 2016. Demographic variables of the donor and recipient as well as clinical variables in pre, intra and post-LT were assessed.
Results: CIIN was described in 39 (22.3%) of recipients. In univariate analysis, history of hepatic encephalopathy ($p = 0.015$), Child score (CIIN group 10 ± 2 vs. Control group 9 ± 2, $p = 0.018$), donor age (65.21 ± 14.40 vs. 56.81 ± 15.73, $p = 0.003$) and pre-LT sodium serum levels (137.55 ± 5.57 mEq/l vs. 135.04 ± 5.25 mEq/l, $p = 0.010$) were associated with CIIN. Patients who underwent LT for hepatocellular carcinoma showed lower rates of CIIN ($p = 0.037$). In multivariate analysis, hepatic encephalopathy (OR 2.679, 95% CI: 1.031–6.116, $p = 0.019$), pre-LT sodium serum levels (OR 1.119 per 1 mEq/l increase, 95% CI: 1.026–1.221, $p = 0.011$) and donor age (OR 1.031 per 1 year increase, 95% CI: 1.004–1.059, $p = 0.025$) were independent risk factors for the development of CIIN. In CIIN group patients had longer Intensive Care Unit [5 (4–10) vs. 4 (4–6) days, $p = 0.023$] and hospital [27 (21–37) vs. 20 (17–32) days, $p = 0.015$] stay, more changes in immunosuppressive treatment (56.4% vs. 19.3%, $p < 0.001$) and more brain radiological imaging technique (15.4% vs. 5.1%, $p = 0.032$) were performed. There were no differences in rates of acute rejection or death at 3 months after LT.
Conclusion: History of hepatic encephalopathy, pre-LT sodium serum levels and donor age are independent risk factor for the development of CIIN after LT. CIIN is associated with an increased use of hospital resources and changes in the immunosuppressive treatment.

BOS435 TYPE OF SURGICAL PROCEDURES AND CLINICAL SIGNIFICANCE OF CALCINEURIN INHIBITOR TEMPORARY DISCONTINUATION REGARDING LT RECIPIENTS UNDERGOING MAJOR ELECTIVE SURGERY

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Background: As patients increasingly have undergone liver transplantation and improved expected survival rate, there is a growing population of LT recipient undergoing elective surgery after LT. However, little has been reported about the types of this surgical procedure or clinical data of immunosuppression protocol during post-operative periods of elective surgery.
Methods: We performed a retrospective study for the type of surgical procedure in 102 recipients who underwent major elective surgery following LT from May 1996 to Dec 2015 at a single institute. In addition, we collected the clinical data associated with immunosuppression during post-operative periods such as status of taking calcineurin inhibitor (CNI), duration of CNI discontinuation, history and number of acute cellular rejection within 3 months after elective surgery during post-operative periods, and trough level of CNI.
Results: There were 102 elective operations, video-assisted thoracoscopic surgery (VATS) was the most common type elective surgery. Median duration

of CNI cessation after heart surgery was median 4 days, the longest duration in total type of elective surgery. We assigned patients to discontinuation group (DG) or continuation group according to status of taking CNI during surgery. DG were 24 recipients and CG were 56 recipients. 22 recipients were excluded due to no use of CNI for immunosuppression already before elective surgery. Recipients occurred biopsy proven acute cellular rejection (BPACR) within 3 months after elective surgery were 2 patients (8.3%) vs. 6 patients (10.7%) in CG vs. DG, respectively ($p = 1.000$). mean tacrolimus trough level were 7.2 ng/ml in CG and 8.6 ng/ml in DG ($p = 0.804$).
Conclusions: If the tacrolimus blood through level was properly maintained, temporary discontinuation during elective surgery in LT recipient was tolerable based on the prevalence of BPACR. Close monitoring for the tacrolimus through level is recommended for LT recipients undergoing elective surgery.

BOS436 SAFETY AND EFFICACY OF A SHORT INDUCTION WITH ANTI-HUMAN T-LYMPHOCYTE IMMUNOGLOBULIN (RABBIT) IN LIVER TRANSPLANTATION IN HIGH RISK PATIENTS

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Background: In liver transplantation (LT), induction by polyclonal antibodies against T lymphocytes reduces risk of rejection or protects renal function by delayed introduction of calcineurin inhibitors. However, this may increase risk of infections. Studies in renal or cardiac transplantation reported that anti T-lymphocyte immunoglobulin Grafalon® (Neovii Biotech, Germany) could be associated with little more rejection but rather less cytomegalovirus (CMV) infection than Thymoglobulin® (Sanofi-Genzyme, France) without difference in survival (Gharekhani et al 2013). This has not been studied in LT. We report our experience of Grafalon® in LT.
Methods: Aim of the study: Safety and efficacy of Grafalon® in liver transplant recipients with high risk of rejection, high MELD score or renal dysfunction. Inclusion criteria: positive crossmatch before LT, MELD score>30, renal insufficiency or retransplantation. Primary endpoint: patient and graft survival. Secondary endpoints: infection and rejection incidence, renal function at month 6, blood cells and lymphocytes counts at day 7, month 1, 3 and 6 post-transplantation. Treatment: Grafalon® 4 mg/kg/day at D0, 3 mg/kg/day from D1 to D4, MMF and Tacrolimus. Corticosteroids are stopped at D90. All patients received CMV and toxoplasmosis prophylaxis.
Results: From July 2016 to February 2017, 38 LT were performed in Bordeaux University hospital. Nine patients were included, 6 with positive crossmatch and 3 with MELD score over 30 (1 with DFG<30 ml/min). Overall patient and graft survival were 88%. One patient died from cardiac arrest unrelated to Grafalon®. 2 rejection episodes were observed. Infections occurred in 77%, most were bacterial and 2 CMV. Evolution of renal function, blood cells and lymphocytes counts are described.
Conclusion: This is the first recent study using Grafalon® in LT. Despite we have included high risk patients, results are positive. They must be confirmed in a larger study.

Clinical Kidney Immunosuppressive agents

BOS437 LONG-TERM PROLONGED-RELEASE TACROLIMUS-BASED IMMUNOSUPPRESSION IN DE NOVO KIDNEY TRANSPLANT PATIENTS: 3-YEAR PROSPECTIVE FOLLOW-UP OF THE ADVANCE STUDY

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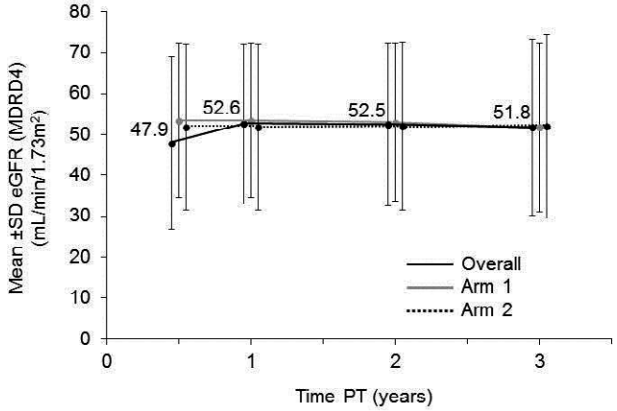
Background: ADVANCE was a Phase IV, 24-week, multicentre, randomised, parallel-group study of two corticosteroid withdrawal strategies in prolonged-release tacrolimus (PR-T)-based regimens for kidney transplant patients. We report 3-year interim data from a prospective, 5-year follow up of ADVANCE (NCT02057484).
Methods: In ADVANCE, adult *de novo* kidney transplant patients received PR-T plus basiliximab, mycophenolate mofetil, and optional intra-operative steroids, and were randomised to receive maintenance steroids to Day 10 (Arm 1), or no maintenance steroids (Arm 2). The follow-up primary endpoint was graft survival. Secondary endpoints were patient survival, estimated glomerular filtration rate (eGFR; Modified Diet in Renal Disease 4 (MDRD4)), acute rejection (AR), biopsy-confirmed AR (BCAR) and adverse events (AEs).
Results: Of 1125 patients enrolled in ADVANCE, follow-up data were obtained for 940 (83.6%). Baseline characteristics for the follow-up population were similar between arms, and to the enrolled population in the original ADVANCE study. Overall Kaplan–Meier (K–M) estimate of graft survival at 1 and 3 years post-transplant (PT) was 94% and 92%, respectively, and patient survival rate was 98% and 96% at 1 and 3 years PT, respectively; both endpoints were similar between arms (Table). Most AR and BCAR occurred ≤6 months PT, with few additional events by Year 3 (Table). Mean eGFR was stable over 3 years PT, and was similar between arms (Figure). of 171 patients assessed for donor-specific antibodies (DSA) at Year 3 PT, 12 (7%) were DSA positive. Overall, 24 (2.6%) patients had AEs considered possibly/probably treatment-related during follow up; none led to treatment discontinuation.
Conclusion: PR-T based immunosuppression was associated with high long-term graft and patient survival rates, and stable eGFR, irrespective of regimen. Rejection rates remained relatively constant after 6 months, and PR-T was generally well tolerated.

Table.

	Patients at risk of graft loss, n*	Patients with graft loss, n	K–M estimate of graft survival, % (95% CI)	Patients at risk of death, n*	Patient deaths, n	K–M estimate of patient survival, % (95% CI)	Patients at risk of AR, n*	Patients with AR episodes, n	K–M estimate of AR-free survival, % (95% CI)	Patients at risk of BCAR, n*	Patients with BCAR episodes, n	K–M estimate of BCAR-free survival, % (95% CI)
6 months post transplant												
Overall	**1125**	**56**	**94.9 (93.6, 96.2)**	**1125**	**14**	**98.7 (98.0, 99.4)**	**1125**	**239**	**78.0 (75.5, 80.4)**	**1125**	**124**	**88.5 (86.6, 90.4)**
Arm 1	552	26	95.2 (93.4, 97.0)	552	8	98.5 (97.4, 99.5)	552	96	81.9 (78.6, 85.2)	552	47	91.1 (88.7, 93.5)
Arm 2	572	30	94.6 (92.7, 96.5)	572	6	98.9 (98.0, 99.8)	572	143	74.2 (70.6, 77.9)	572	77	86.0 (83.1, 88.9)
1 year post transplant												
Overall	**792**	**63**	**94.0 (92.6, 95.5)**	**809**	**22**	**97.7 (96.7, 98.7)**	**618**	**245**	**77.2 (74.7, 79.7)**	**695**	**131**	**87.6 (85.6, 89.6)**
Arm 1	387	30	94.2 (92.2, 96.2)	392	13	97.2 (95.7, 98.7)	313	98	81.3 (78.0, 84.7)	347	49	90.6 (88.0, 93.1)
Arm 2	405	33	93.9 (91.9, 95.9)	417	9	98.2 (97.0, 99.4)	305	147	73.2 (69.5, 77.0)	348	82	84.8 (81.7, 87.8)
3 years post transplant												
Overall	**753**	**80**	**91.9 (90.2, 93.7)**	**770**	**35**	**96.1 (94.8, 97.4)**	**577**	**266**	**74.5 (71.8, 77.1)**	**649**	**155**	**84.4 (82.1, 86.7)**
Arm 1	364	43	90.9 (88.2, 93.5)	368	25	94.1 (91.8, 96.4)	291	111	77.0 (74.1, 81.5)	323	64	86.5 (83.3, 89.6)
Arm 2	389	37	92.9 (90.7, 95.1)	402	10	97.9 (96.6, 99.2)	286	155	71.2 (67.4, 75.1)	326	91	82.5 (79.2, 85.8)

*Number of patients at risk immediately before each time point. **Note:** one patient was not randomised in the ADVANCE study, but was transplanted, treated as if in Arm 1, and included in the overall follow-up population. CI, confidence interval.

Figure.



Overall, N=	939	761	744	746
Arm 1, n=	458	367	355	354
Arm 2, n=	481	394	389	392

Data labels on the graph are for the overall population. Data are not available for all patients at all time points. SD, standard deviation.

BOS438

LONG-TERM PROLONGED-RELEASE TACROLIMUS-BASED IMMUNOSUPPRESSION IN DE NOVO KIDNEY TRANSPLANT PATIENTS: 3-YEAR PROSPECTIVE FOLLOW-UP OF THE ADHERE STUDY

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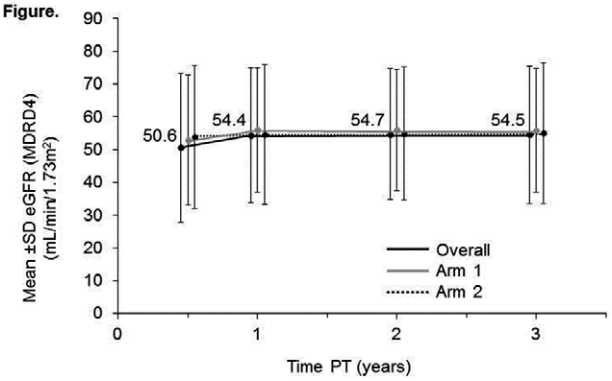
Background: ADHERE was a 52-week, Phase IV, randomised, open-label study of renal function with once-daily, prolonged-release tacrolimus (PR-T) + mycophenolate mofetil (MMF) or sirolimus in *de novo* kidney transplant patients. We report 3-year follow-up data.

Methods: In ADHERE, *de novo* adult kidney transplant patients received PR-T (initial dose: 0.2 mg/kg/day) + MMF (Days 0–27). Patients were randomised on Day 28 to receive PR-T + MMF (Arm 1) or PR-T (reduced dose from Day 42) + sirolimus (1 mg/day) (Arm 2). Steroids were administered throughout. The reported endpoints were estimated glomerular filtration rate (eGFR; Modified Diet in Renal Disease 4 (MDRD4)), graft survival, patient survival, acute rejection (AR), biopsy-confirmed AR (BCAR) and adverse events (AEs). We present 3-year interim data from a prospective, 5-year follow up of ADHERE (NCT02057484).

Results: Of 838 patients enrolled in ADHERE, follow-up data have been obtained for 665. Baseline characteristics were similar between arms. In Arm 2, 181 (60.1%) patients continued to receive sirolimus during follow up. Mean eGFR was stable over 3 years post-transplant (PT), and similar between arms (Figure). Kaplan–Meier (K–M) estimate of graft survival was 93% and 89% at 1 and 3 years PT, respectively, and overall patient survival rate was 98% and 94% PT, respectively; both endpoints were similar between arms (Table). Most AR and BCAR occurred within 6 months PT, with few additional events by Year 3 PT (Table). Overall, 31 (4.7%) patients had AEs considered possibly/probably treatment-related during follow up; two serious AEs led to tacrolimus discontinuation.

Conclusion: PR-T-based immunosuppression for 3 years was associated with stable eGFR, and high long-term graft and patient survival rates, irrespective of whether concomitant treatment was with sirolimus or MMF. PR-T was generally well tolerated.

Figure.



Overall, N=	665	613	499	500
Arm 1, n=	290	283	234	236
Arm 2, n=	301	290	237	236

Data labels on the graph are for the overall population. Data are not available for all patients at all time points. **Note:** not all patients enrolled in the ADHERE study (overall population) were randomised to treatment arms. SD, standard deviation.

Table.

	Patients at risk of death, n*	Patients deaths, n	K–M estimate of patient survival, % (95% CI)	Patients at risk of graft loss, n*	Patient with graft loss, n	K–M estimate of graft survival, % (95% CI)	Patients at risk of AR, n*	Patients with AR episodes, n	K–M estimate of AR-free survival, % (95% CI)	Patients at risk of BCAR, n*	Patients with BCAR episodes, n	K–M estimate of BCAR-free survival, % (95% CI)
6 months post transplant												
Overall	**838**	**9**	**98.9 (98.1, 99.6)**	**838**	**48**	**94.1 (92.5, 95.7)**	**838**	**154**	**80.8 (78.1, 83.6)**	**838**	**85**	**89.4 (87.2, 91.5)**
Arm 1	362	1	99.7 (99.2, 100.0)	362	7	98.1 (96.6, 99.5)	362	61	83.1 (79.3, 87.0)	362	33	90.8 (87.9, 93.8)
Arm 2	368	1	99.7 (99.2, 100.0)	368	8	97.8 (96.3, 99.3)	368	73	80.1 (76.0, 84.2)	368	36	90.1 (87.1, 93.2)
1 year post transplant												
Overall	**741**	**17**	**97.8 (96.8, 98.8)**	**726**	**57**	**92.9 (91.2, 94.7)**	**609**	**158**	**80.3 (77.5, 83.1)**	**665**	**87**	**89.1 (86.9, 91.3)**
Arm 1	349	5	98.6 (97.3, 99.8)	347	12	96.6 (94.7, 98.5)	295	64	82.3 (78.3, 86.2)	318	34	90.6 (87.5, 93.6)
Arm 2	344	1	99.7 (99.2, 100.0)	343	8	97.8 (96.3, 99.3)	280	74	79.8 (75.6, 83.9)	312	37	89.8 (86.7, 93.0)
3 years post transplant												
Overall	**522**	**37**	**94.1 (92.3, 96.0)**	**515**	**79**	**89.0 (86.7, 91.4)**	**425**	**168**	**78.4 (75.5, 81.4)**	**463**	**98**	**87.0 (84.6, 89.5)**
Arm 1	246	13	95.4 (93.0, 97.9)	245	21	93.1 (90.2, 96.0)	206	67	81.1 (77.0, 85.2)	222	37	89.3 (86.1, 92.6)
Arm 2	246	11	95.7 (93.3, 98.2)	246	20	93.1 (90.1, 96.0)	194	81	76.9 (72.4, 81.4)	215	45	86.6 (82.8, 90.3)

*Number of patients at risk immediately before each time point. **Note:** not all patients enrolled in the ADHERE study (overall population) were randomised to treatment arms.

BOS439 CONVERSION FROM TWICE TO ONCE DAILY MELTDOSE TACROLIMUS FORMULATION IN STABLE KIDNEY TRANSPLANT RECIPIENTS: PHARMACOKINETICS (PK) IN LOW TROUGH PATIENTS

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Background: Tacrolimus is a narrow therapeutic index drug; high blood levels have been associated with increased risk of toxicity and adverse events. LCPT (Envarsus®) is a MeltDose®, once-daily prolonged-release formulation of tacrolimus. Previous clinical trials demonstrated that LCPT has greater bioavailability and a "flatter" PK profile when compared to immediate release formulations (TacBID). This post-hoc analysis investigated whether those PK features are conserved in patients with low trough levels (Cmin ≤ 5 ng/ml).
Methods: Data from previous conversion studies (Gaber 2013, Tremblay 2016, Trofe-Clark, submitted) were pooled, and patients with Cmin ≤ 5 ng/ml on one or both products at the time of PK measurements were extracted. The studies were performed with different target conversion rates from TacBID to LCPT (range 1:0.7–1:0.85), and therefore a normalization algorithm was used to allow comparable post-conversion exposure.
Results: 27 patients with LCPT and 26 patients with TacBID had Cmin ≤ 5 ng/ml. Post-normalization $AUC_{0\text{-}24}$ was 148.40 (CV 15.1%) vs. 148.64 (CV 17.5%) ng/ml*h, for LCPT vs. TacBID, respectively (RGM: 1.00 [0.93, 1.07]; p = 0.971). Patients treated with LCPT showed lower peaks (Cmax 10.38 (CV 33.0%) vs. 14.80 (CV 45.7%) ng/ml, respectively; p = 0.001), comparable trough (Cmin 4.40 (CV 17.5%) vs. 4.36 (CV 13.9%) ng/ml, respectively; p = 0.840), and delayed time to peak.
Conclusion: This pooled, post-hoc analysis showed that LCPT maintained its characteristic "flatter" profile also in patients with Cmin ≤ 5 ng/ml (Fig. 1). These results show that converting patients on low dose TacBID to LCPT enables reduction of peak levels, while maintaining comparable exposure and Cmin levels, and supports the broad clinical utility of LCPT.

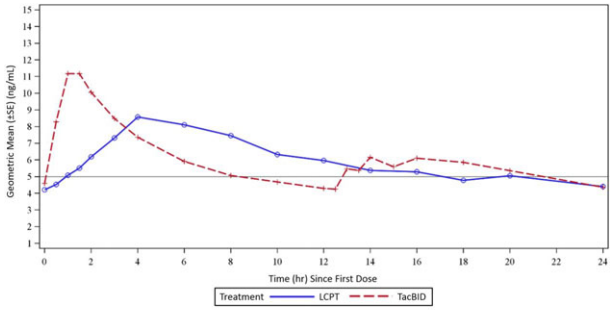

Fig. 1: PK profiles in patients with C_{min} ≤5 ng/mL treated with LCPT (normalized) or TacBID [plot of Geometric means]

BOS440 LOWER INTRAPATIENT THROUGH LEVELS VARIABILITY OF RAPAMYCIN COMPARED WITH EVEROLIMUS

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Background: Immunosuppressive drugs have a narrow therapeutic range and intrapatient blood levels variability must be considered as a prognostic factor. Many studies demonstrate the relationship between the high intra-patient variability of calcineurin inhibitors (CNI) levels and poor long-term renal graft outcome. Recent studies suggest a lower variability when using once-daily tacrolimus compared to the classical twice-daily formulation. Our objective is to analyze the intrapatient variability observed in the blood levels of mTOR-inhibitors (mTORi) and to compare the variability of sirolimus (SRL) with that of everolimus (EVL) in transplant patients converted to an mTORi.
Methods: We analyzed 256 adult renal transplant patients converted to an mTORi between Jan-2009 and Dec-2015 in two Spanish transplant centers. The mean post-transplant conversion time was 51.6 months. One hundred and seventeen were converted to SRL and 139 to EVL. Coefficient of variation (CV) was calculated using at least 3 blood trough levels between 3 and 18 months postconversion. Conversions in the first posttransplant year (121) and later (135) were analyzed separately. CV was correlated with graft evolution (graft survival and/or renal function).
Results: The mean and median CV of the entire group was 25.6 ± 13.0% and 23.7 ± 12.1%. SRL and EVL mean CV was 23.8% and 27.1% (p = 0.04). In the subgroup of late conversions (>1 year) SRL and EVL-CV was 23.0% and 29.0% (p = 0.008). 59.8% vs. 41.7% of patients converted to SRL and EVL respectively had a CV below the median (p = 0.04). No differences in graft evolution could be demonstrated between patients with high and low CV at a mean follow-up of 58.5 ± 21.4 months.
Conclusions: We suggest that SRL has a lower CV than EVL. This difference should probably have a prognostic significance but we have not found differences in the long-term follow up. This might probably be a consequence of that most patients were converted in the stable posttransplant phase.

BOS441 NOCTURNAL DIPPING OF BLOOD PRESSURE IN RENAL TRANSPLANT RECIPIENTS

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Background: There is a marked diurnal variation in blood pressure (BP). Compared with daytime values, BP in most subjects is considerably lower during the night and a 'non-dipping BP profile' is usually defined as a nocturnal SBP fall of less than 10%. Association between non-dipper pattern of circadian rhythm of BP and impaired renal capacity was observed in some studies. A circadian non-dipping pattern is often found in renal transplant recipients, and is related to poor allograft function.
Method/Materials: In this analytic-cross sectional study, 24 h ambulatory blood pressure monitoring (ABPM) was performed in 100 renal post-transplant patients, aged >18 years old, with the serum creatinine level <2 mg/dl after one month of transplant. According to the nocturnal reduction of systolic blood pressure (SBP), dipper (ΔSBP ≥ 10%), non-dipper (0 < ΔSBP < 10%) and reverse dipper (SBP nocturnal rise) pattern were defined.
Result: of 100 participants of this study, 56 patients (56%) were male, and 44 patients (44%) were female. Mean age of participants was 43.34 ± 2.442 years overall, 44.27 ± 2.974 years in males and 42.16 ± 4.074 years in females. Non-dipper pattern was found in 58 patients (58%), revers dipper pattern in 35 patients (35%) and dipper pattern was found only in 7 patients (7%). The nocturnal reduction of systolic blood pressure pattern in participants regarding the gender was not significant (p = 0.794). Mean age of patients with non-dipper pattern was significantly lesser than patients with revers dipper pattern (p = 0.009), but mean age of patients with dipper pattern was not significantly different from patients with non-dipper or revers dipper pattern (p = 0.368, p = 0.605). There was no significant correlation between dipper or non-dipper or revers dipper pattern with immunosuppressive drugs (cyclosporine, tacrolimus and non calcineurin inhibitors), duration of dialysis before transplant, and the time past transplant (p = 0.194).

BOS442 SIMPLIFIED ONCE-DAILY IMMUNOSUPPRESSIVE REGIMEN FOR STABLE KIDNEY RECIPIENTS

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Background: Many immunosuppressive drugs are prescribed as twice-daily dosing. Simplified once-daily dosing of the entire drug regimen can improve treatment satisfaction for patients. We examined the safety, efficacy, and treatment satisfaction of a simplified once-daily immunosuppressive regimen using extended-release tacrolimus, sirolimus, and corticosteroids.
Methods: This study was a prospective, multicenter, controlled, cohort trial. Adult kidney transplant patients with a stable renal function were eligible if they had received transplants more than 3 months prior to study enrollment, and were taking tacrolimus. Efficacy failure, safety, and renal function were evaluated until 6 months post-conversion. Measurements of treatment satisfaction were performed.
Results: A total of 160 kidney recipients were in the intention-to-treat (ITT) population. No graft loss and one patient death at home were reported. The incidence of treated biopsy-confirmed acute rejection until 6 months post-conversion was 0.62%. The mean estimated glomerular filtration rate of was not significantly changed (p > 0.050) but the 24-h urinary excretion of protein before conversion was significantly lower (87.1 ± 140.9 mg/day) than that at 6 months post-conversion (206.5 ± 433.5 mg/day, p < 0.001) in 140 per-protocol (PP) population. Among the ITT population, overall 95 (59.4%) had a type of adverse event (AE) and 28 patients (17.5%) had a serious AE. The patients demonstrated a significant improvements in treatment satisfaction (p < 0.001).

Conclusions: The kidney recipients who received the once-daily immunosuppressive regimen expressed a statistically significant improvement in satisfaction without the additional risks of adverse effects or efficacy failure.

BOS443 COMPARING PLASMAPHERESIS+ IVIG VS. PLASMAPHERESIS+ IVIG+ RITUXIMAB ON MANAGEMENT OF ANTIBODY-MEDIATED ACUTE REJECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: There is no treatment of choice for management of acute antibody-mediated rejection (AMR) in kidney transplant recipients. Plasmapheresis ± intravenous immunoglobulin (IVIg) ± rituximab has been used in different regimens with contradictory results. We compared three regimens of AMR management including plasmapheresis + IVIg ± rituximab in two different rituximab regimens.
Method: In this prospective, observational study kidney transplant recipients with AMR were categorized in three groups. Patients in group 1 were treated with plasmapheresis+ IVIg. Patients in group 2 and 3 received weekly rituximab of 375 mg/m^2 for 4 doses (group 2 or high dose) or 2 doses (group 3 or low dose) in addition to plasmapheresis+IVIg.
Results: Eight, 15, and 9 patients were categorized in groups 1, 2 and 3 respectively. There were no differences between the groups regarding demographic and clinical characteristics of recipients and donors. 10-month grafts' survival (37.5%, 60%, and 37.5% for group 1, 2 and 3 respectively; $p = 0.461$) and patients' survival (75%, 86.7% and 75% for group 1, 2 and 3 respectively; $p = 0.760$) were comparable between groups. Although glomerular filtration rate at month 10 of follow-up did not differ between groups (55.26 ± 20.67, 55.33 ± 20.32, 40.80 ± 18.32 ml/min/1.73 m^2 for group 1, 2 and 3 respectively, $p = 0.411$), however, was about 15 ml/min/1.73 m^2 higher for patients in group 1 and 2 compared to group 3. Late onset neutropenia and interstitial lung disease were developed in some rituximab-treated patients.
Conclusion: Adding high or low doses of rituximab to plasmapheresis+IVIg did not increase 10-month patients' or grafts' survival or level of kidney function in AMR kidney transplant recipients.

BOS444 THE EFFICACY AND SAFETY OF RITUXIMAB AS INDUCTION THERAPY IN KIDNEY TRANSPLANTATION: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: This meta-analysis was undertaken to assess the efficacy and safety of rituximab as induction therapy in kidney transplantation.
Methods/Materials: OVID, Embase, SCI, PubMed and EBSCO were searched till May 2016 to identify randomized controlled trials (RCTs) that used rituximab as induction therapy in kidney transplantation. Major outcomes included rejection, infection, graft survival, and death. The meta-analysis was performed using Review Manager 5.3.5.
Results: Five RCTs met our selection criteria, including 482 kidney transplant recipients. Four of them were multicenter studies. The patients sample size ranged from 13 to 280 and the follow-up duration from 1 to 3 years. The meta-analysis showed that rituximab induction significantly reduced antibody-mediated rejections (2.9% vs. 9.7%; RR = 0.32; 95% CI 0.13–0.76; $p = 0.01$). No significant differences were observed in other efficacy and safety parameters: acute rejection (16.8% vs. 21.1%; RR = 0.80; 95% CI 0.55–1.17; $p = 0.25$), graft survival (94.8% vs. 90.7%; RR = 1.05; 95% CI 0.99–1.10; $p = 0.09$), mortality (2.6% vs. 3.0%; RR = 0.87; 95% CI 0.32–2.37; $p = 0.79$) and cytomegalovirus infection (12.8% vs. 10.0%; RR = 1.29; 95% CI 0.78–2.12; $p = 0.33$), respectively.
Conclusion: It is safe to use rituximab as induction therapy in kidney transplantation, and rituximab induction could significantly reduce antibody-mediated rejection.

Clinical Kidney Donation and Donor Types

BOS445 RE-EVALUATING CUT-OFF POINTS FOR THE EXPANSION OF DECEASED DONOR CRITERIA FOR KIDNEY TRANSPLANTATION IN JAPAN

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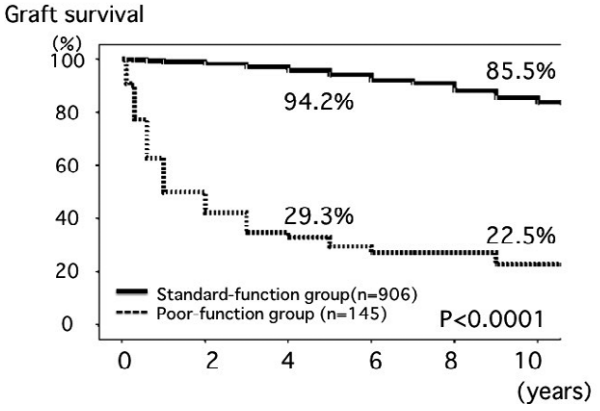
Background: A shortage of donors poses a serious problem for organ transplantation around the world. In response, the concept of the Expanded Criteria Donor (ECD) has been defined to include donors with traditionally less favorable characteristics. That definition has now been accepted and is being applied in kidney transplantation in the United States and Europe. However, the ECD has not yet been defined for deceased donor kidney transplantation in Japan.
Patients and methods: We analyzed data on graft survival and relevant risk factors in patients who received deceased donor kidney transplantation through the East Japan Branch of the Japan Organ Transplant network ($n = 1051$). Recipients were divided into two groups: the standard-function group (estimated glomerular filtration rate (eGFR)≧20 ml/mi/1.73 m^2; $n = 906$) and the poor-function group (eGFR<20 ml/mi/1.73 m^2; $n = 145$) (Cox proportional hazards regression analysis $p < 0.0001$).
Results: The 10-year survival rate was significantly lower in the poor-function group than in the standard-function group (85.5% vs. 22.5%, $p < 0.0001$) (Fig. 1). The two groups differed significantly in recipient and donor risk for graft failure. Recipient risk factors were length of time on dialysis before renal transplantation and incidence of acute rejection after transplantation. Donor risk factors were donor category (heart death), age, history of hypertension, presence of cerebrovascular disease, mean urine output and donor Cr level immediately before donor nephrectomy, total ischemic time, and warm ischemic time.
Conclusion: Data from deceased donor transplantation should be analyzed in depth to determine which factors influence renal function after transplantation. In addition, ECD standards should be reconsidered for use in a Japanese context.

Figure1 Graft survival rate for deceased donor kidney transplantation



Clinical Kidney Ischemia-Reperfusion and Preservation

BOS446 THE EFFECT OF MANNITOL IN LIVING DONOR RENAL GRAFT FUNCTION

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Background: The only setting in which the mannitol is thought to be a useful renal protectant is in *renal Transplantation*, However, much of the work was completed in the 1980s and early 1990s. And according to some investigators most of these studies lack scientific rigors.

Material and methods: The study included 30 recipients divided into two groups according to their living donors. Each consists of 15 patient: In group 1 the donor-received mannitol 20% solution, at a dose of 0.5 mg/kg IV infusion intraoperative 30 minute before vascular clamp. The other group received routine intra-operative fluids. Follow-up data of early postoperative graft function were collected over 14 days, and at 1, 2, and 3 months.
Results: The total urine volume 'was higher' at the end of surgery and in first two postoperative days in the mannitol group [p values of 0.046 at the end of surgery and 0.047 & 0.032 in the first & second post-operative days respectively]. Serum creatinine for recipients of mannitol group recovered to normal range more early than the other group [p value 0.038]. Serum creatinine was lower post-operatively in the mannitol group, but these differences remained statistically significant only for the first 7 post-operative days [p value is 0.018, 0.001, 0.027, 0.015, 0.009 at the end of surgery and on days 1, 2, 3, 7 respectively]. Also mean creatinine clearance of mannitol group was significantly higher for each of the first post-operative 7 days, then showed no statistical differences in post operative day 14, and at one, two and three months [p value was 0.425]. The rejection of renal graft occurred only in two patients, one in each group, but the one occurring in the mannitol group was obviously due to a surgical technical problem.
Conclusion: According to our study, mannitol allows safety passage of early but critical period of graft life. However, mannitol seems to have a little or no effect later on as regards renal graft function.

BOS447 RENAL TRANSPLANT ISCHEMIA/REPERFUSION INJURY CORRECTION WITH CYTOKINES ADSORPTION: EARLY AND LONG-TERM RESULTS

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Cellular metabolism inadequacy in terms of hypoxia upon organ conservation leads to nephron injury.

Cytokines play the leading role in pathogenes of renal transplant ischemia/reperfusion injury.

We conducted a prospective randomized clinical trial. We applied coupled plasma filtration and adsorption (CPFA) in 33 patients of study group. After the operation each patient had one such procedure. In the control group there were 33 patients who received paired transplants. All 66 transplants were received from expanded criteria donors.

Ischemia/reperfusion is followed by a significant release of cytokines (TNF, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70) into blood that was observed in patients of control group. In addition to this, maximum peak was recorded 4–6 h after reperfusion. Moreover, a significant relation with conservation duration and thermal ischemia was observed. In patients of the study group cytokine concentration remained stable. Even 5 days after transplantation cytokine concentration was significantly lower than in control group. In patients of the main group transplant function improvement was observed: a higher rate of diuresis and GFR, blood creatinine improvement, microcirculation improvement.

CPFA has no effect on tacrolimus blood concentration.

3 months after transplantation patients of the main group had a significantly lower level of daily proteinuria ($p > 0.001$); 6 months – higher GFR ($p = 0.02$) and lower daily proteinuria ($p = 0.02$). 1 year after transplantation patients of the main group had lower creatinine plasma level ($p = 0.001$), higher GFR ($p = 0.001$), daily proteinuria 2.5 times lower ($p = 0.001$) vs. patients of control group.

However, we believe that the selective removal of cytokines in the early postoperative period after kidney transplantation is an effective and necessary procedure and it may reduce the ischemia / reperfusion injury severity and improve outcomes of renal transplantation with transplants received from expanded criteria donors.

Basic Kidney Ischemia-reperfusion and preservation

BOS448 ISCHEMIA REPERFUSION INJURY CAUSES LOCAL RELEASE OF FREE HEME WHICH AGGRAVATES ACUTE KIDNEY INJURY

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Background: Ischemia reperfusion injury is linked to solid organ transplantation and causes local vasoconstriction and blood stasis. Locally, release of toxic extracellular hemoglobin (hb) and free heme contribute to acute organ injury. In this study, generation of free heme in renal ischemia reperfusion injury (IRI) was investigated in a mouse model.
Methods: IRI was induced by 15, 35 and 45 min renal pedicle clamping in mice. Sham surgery served as control. Mice were sacrificed at 2 and 4 h after IRI. Free heme was measured in the renal tissue as well as in the circulating blood. qPCR for pro-inflammatory cytokine expression, histology and immunohistochemistry for acute kidney injury and inflammation were done.
Results: In correlation with duration of ischemia the free heme generation in the tissue increased. The contralateral kidney which was not clipped served as a control in these experiments. By increasing ischemia time the local renal tissue damage aggravated and more pro-inflammatory cytokines (TNF-alpha, MCP-1, IL-6) were produced. In addition, enhanced neutrophil infiltration correlating with enhanced ischemia time was observed.
Conclusion: Prolonged ischemia times correlate with enhanced release of free Hb and free heme in the tissue and aggravate IRI. Strategies to bind free heme in IRI would be promising in future studies.

Clinical Kidney Ischemia-reperfusion and preservation

BOS449 DONOR REMOTE ISCHEMIC PRECONDITIONING DOES NOT IMPROVE KIDNEY TRANSPLANT OUTCOME

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Remote ischemic preconditioning (RIPC) is proposed to reduce ischemia-reperfusion injury in kidney transplant recipients. All available studies describe the results of RIPC applied to the recipients at various time points after transplantation procedure. We investigated whether RIPC applied to the deceased donors before organ retrieval would influence kidney transplantation outcome.
Material/Methods: 46 deceased donors (age 46.9 ± 15.9 years, 21F/26M, KDRI 1.49 ± 0.47, donor serum creatinine 1.23 ± 0.45 mg/dl) were included in the study. RIPC was performed by provoking lower limb ischemia through temporal closure of iliac artery in 17 donors (age 49.2 ± 18 years, median 58 years, 7F/10M, KDRI 1.60 ± 0.47, median 1.46). Control group included 29 donors (age 45.3 ± 15.0 years, median 46 years, 14F/15M, KDRI 1.45 ± 0.46, median 1.37). Kidneys were received by 88 recipients (age 50.5 ± 13.9 years, 30F/58M, hospitalized 21 ± 16 days post Tx) after 1568 ± 358 min cold ischemia time.
Results: The groups were donor age and KDRI matched but the RIPC group included significantly more donors after cerebrovascular accident (CVA) compared to the control group (11, 65% vs. 7, 24%; $p = 0.016$). Delayed graft function (DGF) was significantly more prevalent in RIPC group (12/39% vs. 6/11%; $p = 0.004$). All cases of DGF in the control group were observed in recipients who received their grafts from CVA donors, whereas in RIPC group DGF was present in 8 recipients from CVA donors and in 4 from non-CVA donors.

Short-, as well as long-term, allograft function (eGFR ml/min) was not affected by the RIPC procedure (1-month: 42.5 ± 17.8, median 42 vs. 47.9 ± 19.7, median 48; 1-year: 52.1 ± 17.9, median 57 vs. 52.9 ± 17, median 54; 4-year: 57.1 ± 24.0, median 62 vs. 58.9 ± 12.5, median 58).
Conclusion: Remote ischemic preconditioning performed in kidney donors before organ retrieval does not influence short- nor long-term allograft function. Moreover it is related to the higher incidence of delayed graft function.

Basic Kidney Ischemia-reperfusion and preservation

BOS450 ERK AND HIF1 PLAY A MAJOR ROLE IN HYPOTHERMIC PROTECTION AGAINST RENAL ISCHEMIA-REPERFUSION INJURY

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Backgrounds: Hypothermia attenuates the renal injury induced by ischemia-reperfusion. However, the detailed molecular pathway remains unknown. It has been reported that hypothermia may induce ERK and HIF1 in various cellular injury model. We evaluated the role played by ERK and HIF1 in hypothermic protection against renal ischemia-reperfusion injury.
Methods: C57Bl/6 mice were divided into the following groups: sham-operated (cold, 32°C) vs. normal temperature (37°C); ischemia-reperfusion mice (32°C vs. 37°C); and PD98059- or vehicle-treated ischemia-reperfusion mice (32°C). Kidneys were harvested 10 and 27 min after induction of renal

ischemia and 24 h after ischemia-reperfusion injury. Functional and molecular markers of kidney injury were evaluated.
Results: The blood urea nitrogen and serum creatinine levels and the histologic renal injury scores were significantly lower in 32°C ischemia-reperfusion than 37°C ischemia-reperfusion kidneys (all p values < 0.05). The expression levels of Bax and caspase-3 and the extent of TUNEL and 8-OHdG cell positivity decreased, whereas the renal Bcl-2 level increased, in 32°C ischemia-reperfusion compared to 37°C ischemia-reperfusion mice. The extent of renal ERK phosphorylation was significantly higher in ischemia-reperfusion than sham-operated kidneys. Also, ERK phosphorylation was significantly increased in the kidneys of 32°C compared to 37°C ischemia-reperfusion mice. PD98059 treatment of 32°C ischemia-reperfusion mice significantly decreased the renal HIF-1 level ($p < .05$) and increased the BUN, s-Cr, renal Bax, and caspase-3 expression levels; the tissue injury score; and the proportions of TUNEL- and 8-OHdG–positive cells. PD98059 also increased the renal Bcl-2 level in such mice.
Conclusion: Hypothermia attenuates the renal apoptosis and oxidative stress induced by ischemia-reperfusion via a mechanism involving ERK and HIF1 activation.

BOS451 OMEGA-3 FATTY ACID AMELIORATES RENAL ISCHEMIA REPERFUSION INJURY VIA AUTOPHAGIC FLUX

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Background: Recently, it is reported that Omega 3 regulates the autophagy. Using fat-1 transgenic mice, a well-established animal model that endogenously synthesizes Omega 3 fatty acid, we evaluated whether ω3-PUFA may attenuate ischemia reperfusion (IR) injury, and evaluated associating mechanism.
Methods: C57Bl/6 background fat-1 mice and wild type mice were divided into 4 groups; wild type sham, fat-1 sham, wild type IR (reperfusion 35 min after clamping of both renal artery and vein) renal injury, and fat-1 IR renal injury. Kidneys and blood were harvested 24 h after IR injury. Real time RT-PCR, western blot and immunohistochemistry for molecular study and H&E stain and PAS stain for histologic examination were performed.
Results: Fat-1 IR mice kidney showed improvement of renal cell survival, renal function, and pathologic damage compared to wild-type (WT) mice kidney. Also, fat-1 IR mice kidney showed the decreased oxidative stress and apoptosis. Compared to WT IR mice kidney. WT IR mice kidney higher amounts of LC3, Beclin-1, Atg7 and p62, compared to sham mice kidney. Fat-1 IR mice kidney showed higher amounts of LC3, Beclin-1 and Atg7 and lower amounts of p62 compared to WT IR mice kidney. In addition, renal cathepsin D and ATP6E were also increased in fat-1 IR mice kidney compared to WT IR mice kidney. Further, there was also increased AMPK activation in fat-1 IR mice kidney. AMPK activation led to inhibition of phosphorylation of the mechanistic target of rapamycin (MTOR) in fat-1 IR mice kidney.
Conclusion: Omega 3 fatty acid in fat-1 mice as contributing to AMPK-mediated autophagy activation leading to a reno-protective response, as a novel kidney defense mechanism.

BOS452 THE EFFECTS OF GLUTATHIONE SUPPLEMENTATION ON KIDNEYS UNDERGOING HYPOTHERMIC MACHINE PERFUSION

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Background: Reduced glutathione is a constituent of perfusion fluids commonly used for hypothermic machine perfusion (HMP) of kidneys prior to transplantation (e.g. KPS-1). Glutathione acts to reduce damage to tissue by scavenging free radicals produced during ischaemia. Previous research by our unit suggests reduced glutathione levels are depleted quickly during HMP and are almost undetectable after 12 h.

The aim of this study was to investigate the effect of supplemental reduced glutathione on perfusate metabolite concentrations over 18 h of hypothermic machine perfusion.
Methods: This study utilised a paired study design, using porcine kidneys ($n = 7$) in a donation after cardiac death (DCD) model of renal transplantation. Machine perfusion fluid in the experimental arm was supplemented with 7 mM additional reduced glutathione (i.e. 10 mM total vs. 3 mM).

The metabolic profile of kidneys perfused with standard (S) vs. reduced glutathione-supplemented (GS) perfusion fluid was characterised using one-dimensional nuclear magnetic resonance spectroscopy (1D-^{1}H NMR).
Results: As expected, the reduced glutathione concentration in the perfusion fluid was higher at all time points in the GS group, compared with the controls ($p < 0.01$), with easily detectable levels even after 18 h of HMP (mean 0.24 mM). In addition, fifteen metabolites demonstrated significant differences between the two arms of the experiment. Citrate, glutamate and glycine concentrations were higher in the GS group ($p < 0.05$), whereas lactate concentrations were higher in the S group ($p < 0.05$).
Conclusion: The protective antioxidant glutathione was present in the perfusion fluid even following periods of prolonged HMP when supplemented initially. Furthermore, the perfusate of kidneys perfused with GS fluid displayed a different metabolic profile to control kidneys. This indicates that the presence of more reduced glutathione in the perfusion solution modifies metabolic pathways in the kidney during HMP.

BOS453 PERIPHERAL ISCHAEMIC PRECONDITIONING – A METHOD TO REDUCE KIDNEY ISCHAEMIA REPERFUSION INJURY

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Background: Ischaemia-driven Acute Kidney Injury (AKI) is a common outcome following surgery. During AKI, the kidney becomes temporarily starved of oxygen and nutrients, resulting in Ischaemia Reperfusion Injury (IRI). Repetitive short durations of ischaemia have been reported to render the kidney resistant to a subsequent prolonged IRI, termed Ischaemic Preconditioning (IPC). We have successfully demonstrated that IPC applied directly to the kidney prior to IRI improves functional and histological outcomes (Localised Ischaemic Preconditioning). We will describe the experimental transition to a Aortic-IPC model as a method to reduce IRI.
Methods/Materials: Thirty male Lewis rats were assigned to groups ($n = 6$ per group). Groups included, Sham, IRI only (direct clamping of renal vessels for 45 min then release) or IPC + IRI.

The IPC method was either applied to the renal vessels or the Aorta. In brief, the vessels were occluded for 2-min ischaemia, 5-min reperfusion for 3-cycles prior to IRI (2/5 approach). In the Aortic model the IPC window was also extended to include a 5-min ischaemia, 5-min reperfusion for 3 cycles group (5/5 approach). Renal tissue and blood serum was collected at 48-h post recovery to assess renal injury.
Results: IRI injury resulted in a creatinine rise relative to sham (33.8 and 65.7 μmol/l respectively, $p < 0.001$). Direct IPC (2/5) and Aortic IPC (2/5 and 5/5) improved creatinine relative to IRI alone (37.9, 40.4 and 43.7 μmol/l respectively, $p < 0.001$). Histological damage was improved in the direct IPC (2/5) model and the aortic (2/5) model.
Conclusion: We have demonstrated functional and histological improvements in AKI severity using B.IPC and A.IPC prior to IRI. Given the challenges implementing successful IPC in clinical trials a detailed understanding of the molecular mechanisms is required. The transition to an Aortic IPC approach will allow study into the molecular mechanism which may be circulated in the blood.

Basic Cell Ischemia-reperfusion and preservation

BOS454 P66SHC: A DRUGGABLE TARGET IN THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY (IRI)?

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Background: Excessive production of reactive oxygen species (ROS) has been causally linked to the development of ischemia/reperfusion injury (IRI) during solid organ transplantation. Antioxidants largely failed in the clinic and direct inhibition of key ROS producing system is not yet clinically feasible. p66Shc is unique among ROS producing systems as its knockout did not affect normal survival while it prevented pathophysiological conditions caused by excessive ROS production. In our work we devise strategies to target signaling pathways, which control the activation of ROS producing systems, for the prevention of IRI.
Material and methods: Various cellular models and conditions were used to simulate ischemia-reperfusion in vitro. P66Shc regulation by signaling pathways was addressed by using immunoblot analyses, mass spectrometry, mutagenesis and reconstitution assays in wild-type and p66Shc-deficient cells.
Results: Previous work suggested that the activation of the pro-oxidant and pro-death function of p66Shc required phosphorylation on serine 36 (S36) followed by mitochondrial import. We performed a detailed analysis of the mechanisms controlling p66Shc activation and function. In our work we could confirm the requirement of PKCβ for ROS production and cell death but not for

p66ShcS36 phosphorylation. Our search for a *bona fide* S36 kinase lead to JNK1/2, whose involvement was confirmed through the use of inhibitors and JNK1/2-deficient cells. Moreover, expression of a S36E mutant in p66Shc-deficient cells restored ROS production under the stress conditions tested here. Additionally, we identified S139, T206 and S213 as critical PKCβ target sites regulating the pro-oxidant and pro-death function of p66Shc.
Conclusions: In our work we established the conditions for future therapeutic inhibition of the oxidoreductase p66Shc, a main contributor to pro-oxidant damage during ischemia and reperfusion.

Basic Heart Ischemia-reperfusion and preservation

BOS455 TREATMENT WITH ATGS BEFORE REPERFUSION REDUCE VASCULAR INFLAMMATORY RESPONSE IN HUMAN VESSELS

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Introduction: Polyclonal antithymocyte globulins (ATGs) are immunosuppressive drugs widely used in induction of immunosuppression and treatment of acute rejection. Previously, we demonstrated that ATG bind to endothelial cells in vivo. We investigated the effect of the early application of ATGs on the vascular response of human vessels after ischemia-reperfusion.
Material and methods: Human vessels (saphenous vein/internal thoracic artery segments discarded from coronary by-pass surgical procedures) were obtained after informed consent and Ethics approval. The vessels were preserved in a NaCl/Heparin solution and after 4 h ischemia connected to a customized bioreactor consisting on a double roller-pump with oxygenator and reperfused for 120 min with compatible human blood. Vessels were treated with 1 mg/kg ATG (Thymoglobulin® Sanofi-Aventis, France). Untreated vessels served as control group. Blood samples were obtained during the reperfusion and biopsies obtained at the end of the experiment. Vitality of the vessels was measured through oxygen consumption during reperfusion. Cytokines (IL-6, TNF-alpha) as well as VEGF were analysed by ELISA. Immunohistochemical analysis of CD11 and CD31 was performed to evaluate the reduction of the vascular inflammation.
Results: Vitality of the vessels could be demonstrated with adequate oxygen consumption and stable pH values. Treatment with ATGs prevented increase of IL-6 in serum. No differences regarding the concentration of TNF-alpha and VEGF were observed within the groups. Immunohistochemical analyses showed a significant reduction of positive reactions to CD11b and CD31 after treatment with ATG when compared to control vessels.
Conclusion: Down-regulation of adhesion molecules by ATG may be responsible for decreased expression of CD11b and CD31 after reperfusion. We could demonstrate lower cellular infiltration and modulation of endothelial response, in spite of little activity on circulating pro-inflammatory cytokines.

Translational Kidney Ischemia-reperfusion and preservation

BOS456 EARLY APPLICATION OF MTOR INHIBITORS REDUCE VASCULAR INFLAMMATORY RESPONSE AFTER ISCHEMIA-REPERFUSION INJURY

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Background: Ischemia reperfusion injury is associated with serious inflammatory responses. Inflammation triggers mononuclear cells to migrate through vessel walls leading to tissue damage. We aimed to investigate the effect of the early application of Everolimus and Sirolimus on the vascular response of human vessels after ischemia and posterior reperfusion.
Methods: Human vessels (saphenous vein/internal thoracic artery segments) were obtained after informed consent and Ethics approval. The vessels were preserved in a NaCl/Heparin solution and after 4 h ischemia connected to a customized bioreactor consisting on a double roller-pump with oxygenator and reperfused for 120 min with compatible human blood. The vessels were treated with Everolimus (10 ng/ml Certican® Novartis, Switzerland) or Sirolimus (10 ng/ml Rapamune, Pfizer, USA). Untreated vessels served as control group. Blood samples were obtained during the reperfusion and biopsies at the end of the experiment. Vitality of the vessels was measured through oxygen consumption during reperfusion. Inflammatory cytokines (IL-6, TNF-alpha) as well as VEGF were analyzed by ELISA. Immunohistochemical analysis of CD11 and CD31 was performed to evaluate the vascular inflammation.
Results: Vitality of the vessels could be demonstrated with adequate oxygen consumption and stable pH values. Treatment with Everolimus showed a significant reduction of IL-6 in comparison to Sirolimus and control vessels, and of TNF-alpha compared to Sirolimus at the end of the reperfusion. No differences regarding the concentration of VEGF were observed. Immunohistochemistry showed a significant reduction of positive reactions to CD11b and CD31 in both mTORs compared to control vessels.
Conclusion: Early treatment with mTOR inhibitors, especially Everolimus, may prevent the pro-inflammatory reaction after ischemic injury. Both Everolimus and Sirolimus reduce the cellular infiltration and the vascular response after reperfusion.

Basic Liver Ischemia-reperfusion and preservation

BOS457 EXTRACELLULAR VESICLES DEPRIVED FROM MESENCHYMAL STEM CELLS ALLEVIATED LIVER ISCHEMIA-REPERFUSION INJURY BY SUPPRESSING THE ACTIVATION OF RHOA-ROCK PATHWAY

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Objects: Several studies indicate that mesenchymal stem cells (MSCs) have protective effects against various cellular-injury models. The mechanism of this protection was identified mainly depend on extracellular vesicles (EVs) secreted from MSCs. However, the exact mechanism has yet to be elucidated. This study try to investigate the protective effect of MSCs derived EVs (MSC-EVs) against hepatic ischemia-reperfusion injury in rats.
Methods: EVs were isolated from conditioned medium of MSCs by ultracentrifugation. MSCs-EVs were co-cultured with human normal liver cell line LO2 in the model of hypoxia/reoxygenation to evaluate the protective effects of MSCs-EVs. Concurrently, MSCs-EVs were also injected via the portal vein in a C57BL/6 mice model of 70% warm hepatic I/R injury to evaluate the therapeutic effect of MSC-EVs transplantation.
Results: MSC-EVs infusion significantly prevent liver enzyme release and improve the acutely injured liver in histology. The levels of the hepatocyte injury markers AST and ALT were significantly lower in the MSC-EVs group than that in the control group at different reperfusion time. In vitro assays demonstrated that MSC-EVs promoted hepatocyte proliferation and had a direct inhibitory effect on hepatocyte apoptosis induced by hypoxia/reoxygenation. Furthermore, our study showed that the prevention of RhoA-ROCK pathway activation played a pivotal role in the protection.
Conclusions: Our results demonstrated that MSCs-EVs alleviate hepatic I/R injury both in vivo and in vitro. It could be a promising therapeutic strategy to alleviate hepatic ischemia/reperfusion injuries after liver transplantation.
Keywords: Mesenchymal stem cells. Extracellular vesicles Ischemia reperfusion injury.

Basic Others Ischemia-reperfusion and preservation

BOS458 THE IMPACT OF SIMVASTATIN DONOR THERAPY ON CHRONIC ALLOGRAFT VASCULOPATHY; INVESTIGATIONS IN A MURINE AORTIC TRANSPLANTATION MODEL

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Previous studies have shown that a single donor-donor therapy with tetrahydrobiopterin (BH4) prevents from deleterious effects of ischemia-reperfusion injury in a murine pancreas transplantation model. Since BH4 is approved only for treatment of phenylketonuria, we herein aimed to investigate, if a single donor therapy with simvastatin is able to enhance BH4-bioavailability and protects from IRI-associated chronic allograft vasculopathy.

In the heterotopic murine aortic transplantation model male BALB/c mice served as donors and male C57Bl6-mice as recipients. Donors were either pretreated with an oral dosage of 5 mg/kg b.w. Simvastatin 2 h before organ

retrieval or remained untreated. All grafts were subjected to 24 h of cold ischemia time (CIT) before transplantation. Following either 2 h or 28 days of reperfusion, grafts were retrieved and mRNA expression of vWF, eNOS, GTPCH and GCH1 was analysed by RT-qPCR. eNOS monomer/dimer formation was detected by western blot and intragraft BH4-levels were determined by HPLC. Furthermore, all grafts were histologically assessed in H&E stained tissue.

Compared to controls, simvastatin resulted in a markedly reduced expression of vWF, however, not influencing GTPCH- and GCH1 expression. Following 2 h of reperfusion, Simvastatin-treated grafts displayed markedly higher BH4-levels compared to vector-treated grafts. ($p = 0.056$). These differences were not significant following 28 days. Following 28 days of reperfusion a significantly higher eNOS monomer/dimer ratio was determined compared to grafts reperfused for 2 h, independently from treatment ($p < 0.05$). Finally, following 28 days significantly less thrombotic events were observed in simvastatin-pretreated grafts compared to the respective untreated grafts ($p < 0.05$).

We could not confirm the hypothesis, that a single donor simvastatin treatment directly influences BH4-biosynthesis. However a protective effect could be observed, which needs further investigations.

Clinical Kidney Rejection

BOS459 SIGNIFICANT IMPACT OF C3D BINDING WITH DE NOVO HLA-DRB3-5 AND DQ DONOR-SPECIFIC ANTIBODIES ON ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Recent evidence suggests that HLA class II *de novo* donor-specific antibodies (dnDSA) with complement binding activity are associated with antibody-mediated rejection (AMR) following kidney transplantation. We examined the complement binding characteristics of dnDSA in relation to AMR.
Methods: We evaluated the characteristics of HLA class II dnDSA and their C3d binding activities using dnDSA-positive sera from 15 kidney transplantation recipients with AMR.
Results: Seven of 20 DRB1 (35%), 10 of 15 DRB3-5 (67%), and 15 of 20 DQ (75%) was dnDSA positive, respectively. C3d positivity in the positive dnDSA was also noted in 3 of 7 DRB1 (42.9%), 9 of 10 DRB3-5 (90%), and 13 of 15 DQ (86.7%), respectively, which demonstrated a significantly higher rate of positivity in C3d for DRB3-5 and DQ as compared to those for DRB1 ($p = 0.038$ and <0.001). The mean MFI value for C3d in the positive dnDSA was predominantly higher for DRB3-5 (dnDSA-positive: 21057, dnDSA-negative: 6754, $p = 0.027$) and DQ (positive: 19144, negative: 1056, $p = 0.001$), while that for DRB1 was not (positive: 7924, negative: 4549, $p = 0.222$).
Conclusions: Regarding the association of HLA class II dnDSA related to AMR, our findings suggested that dnDSA for DRB3-5 and DQ have an elevated risk of AMR, as well as C3d binding activities as compared to DRB1.

BOS460 THE EARLY OUTCOMES OF RECIPIENTS WITH PRE-TRANSPLANT DONOR-SPECIFIC ANTIBODIES IN CROSSMATCH NEGATIVE RENAL TRANSPLANTATION

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Background: Preformed donor specific antibodies (DSA) have shown to increase the risk of AMR and have a deleterious effect on kidney graft survival, even in the presence of a negative crossmatches.
Methods: Between January 2015 and October 2016, 335 patients received kidney transplantation from ABO compatible living donor. Among them, 56 (16.7%) had preformed DSA and crosshatch negative. We divided them two groups: Desensitization group ($n = 14$) received rituximab (200 mg) and plasmapheresis before the surgery and Control group ($n = 42$) did not receive any treatment. Before and after surgery, DSA were analyzed by Luminex assay, and the renal function was analyzed during the follow-up periods.
Results: The baseline PRA of Desensitization group was significantly higher compared to those of control group. During the follow-up periods, the sCr was lower in Desensitization group until 1 month after transplantation. However, after then, sCr was not significantly different between two groups. And eGFR was not significantly different between two groups. However, sCr and eGFR showed the tendency that those of D-group were consistently low compared to those of control group, even though it is not statistically significant. The clinical rejection was developed in 8 patients (D-group: 2, C-group: 6). And there was no AMR. The PRA of Class I was significantly decreased in D-group (preop 43.45 vs. postop 18.73), and the MFI of DSA was significantly decreased in all group, respectively (preop. Vs. postop, 2875.6 vs. 846.6 in D-group, $p = 0.009$; 2762.8 vs. 1119.4 in C-group, $p = 0.025$).
Conclusion: Although not statistically significant, sCr shows a lower pattern and eGFR shows a higher pattern in Desensitization group than in Control group during the early periods. And preoperative desensitization for DSA can lower the MFI of DSA in early periods. So, we assumed that preoperative desensitization may be available to reduce the AMR and increase the graft outcome.

Translational Kidney Histology

BOS461 ANALYSIS OF INFILTRATING T CELLS IN ACUTE T CELL-MEDIATED REJECTION IN THE KIDNEY TRANSPLANT (ATCMR-KTX)

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Background: The diagnosis of acute T cell-mediated rejection in the kidney transplant (ATCMR-KTx) is based on the estimation of mononuclear cell infiltration instead of the quantification of the different T cell subsets mediating rejection. Therefore, a more detailed analysis of the cellular inflammatory infiltrate in ATCMR-KTx is expected to improve the diagnostic accuracy of the Banff classification. Thus, our main aims were (1) to compare the differential immune T cell subset composition in patients with ATCMR-KTx with that of the absence of rejection, and (2) to explore the association of their respective immune profiles with kidney transplant outcomes.
Methods/Materials: A pilot cross-sectional immunohistochemical analysis of the cellular infiltrate was performed in 14 patients with biopsy-proven ATCMR-KTx and 7 patients with no rejection in their biopsy, who were then followed up to 54 months to explore the association of their immune infiltrates with kidney transplant outcomes, including deterioration of kidney transplant function, further rejection episodes and transplant loss.
Results: In a comparison to the absence of rejection, ATCMR-KTx was characterised by numerical dominance of cytotoxic T lymphocytes over Foxp3+ regulatory T cells, but did not reach statistical significance due to our small sample size. There was no obvious difference in absolute numbers of infiltrating cytotoxic T lymphocytes, Foxp3+ regulatory T cells and Th17 cells between the two patient groups when quantified separately. Our exploratory analysis on associations of T cell subset quantifications with kidney transplant outcomes revealed that the degree of Th17 cell infiltration was significantly associated with shorter time to doubling of creatinine and time to transplant loss.
Conclusions: Although this was a small pilot study, results support our suspicion that the immune balance in ATCMR-KTx is tilted towards the pro-rejection forces and prompt larger more sophisticated studies.

Clinical Kidney Rejection

BOS462 PERIPHERAL BLOOD LYMPHOCYTE SUBSETS IN THE DIAGNOSIS OF CHRONIC RENAL ALLOGRAFT REJECTION

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The percentage of different lymphocyte subsets and their ratio indices in peripheral blood of kidney transplant recipients reflect the state of the immune system and its response to the allogenic organ, The purpose of our study was to examine the possibility of using these indicators for non-invasive diagnosis of chronic allograft rejection, Subsets of peripheral blood lymphocytes: T cells (CD3+, CD19-), T-helper cells (CD3+, CD4+), T-cytotoxic (CD3+, CD8+), T-activated (CD3+, HLA-DR +), NK-T cells (CD3+, CD16+56+), B cells (CD3-, CD19+, HLA-DR +), NK cells (CD3-, CD16+56+) and their ratio indices were studied by flow cytometry in 43 patients 1–9 years (mean – 3.2 years) after kidney transplant: 23 recipients with normal renal function (group 1) and 20 – with biopsy proven chronic rejection (group 2), The control group included 23 healthy donors, Only activated T lymphocytes in both groups were significantly higher than in the control group (8.9%; 8.4%; 6.8% respectively, $p < 0.05$). The mean values of NK-T cells and B cells in group 2 were significantly decreased in comparison with group 1 (2.4%; 5.6% and 9.6%; 12.4% respectively, $p < 0.05$), Analysis of ratio indices of different lymphocyte subpopulations in the groups

compared revealed a significant increase in group 2 compared to group 1 of the following indices: T cells / NK-T cells index (46.9 vs. 22.5, $p < 0.05$) and T-activated / B cells (4.2 vs. 1.1, $p < 0.05$). The obtained data can be used for non-invasive diagnosis of chronic rejection. Furthermore, natural killer T cells can synthesize and secrete cytokines of both the Th1 and Th2 profiles, thereby performing important regulatory functions, limiting the intensity of inflammation and immune response to prevent hyperergic reactions. A decrease in the level of this lymphocyte subpopulation can play a role in the pathogenesis of chronic renal allograft rejection.

Translational Kidney Rejection

BOS463 EARLY ISOLATED V-LESION MAY NOT TRULY REPRESENT ACUTE REJECTION

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Background: Acute vascular rejection (AVR) is known to be a negative prognostic factor for kidney allograft survival. However, role of isolated v-lesion (IV) defined as intimal arteritis with minimal tubulointerstitial inflammation is unclear. While some authors believe in hidden ischemic/reperfusion injury, others are convinced of its rejection origin. Current Banff classification assesses IV as type 2 or 3 acute T-cell mediated rejection and/or antibody-mediated rejection. To help resolve if IV truly represents acute rejection, molecular profiling of IV and T-cell mediated vascular rejection (TCMRV) was performed.
Methods/Materials: Transcriptome of early IV and TCMRV was compared using microarrays (Illumina Human HT-12 v4 Expression BeadChips). Differentially expressed genes were defined as those with fold change >2 and adjusted p-value <0.05 corrected for multiple testing. The enrichment of deregulated genes in biological processes was analysed using DAVID database.
Results: Differential gene expression analysis generated a candidate list containing 95 differentially expressed probe sets. Genes encoding chemokines, T and B- lymphocyte associated transcripts, regulators of adaptive and innate immune response were upregulated in TCMRV. Gene-term enrichment analysis identified these genes to be significantly enriched with GO terms and KEGG pathways predominantly associated with immune and inflammatory response (Table 1).

Table 1: GO terms and KEGG pathways enriched in TCMRV vs. IV.

	GO term	p (Benjamini)
GO: 0006955	immune response	2.88E-05
GO: 0006954	inflammatory response	6.6E-03
GO: 0001775	cell activation	1.68E-0.2
GO: 0009611	response to wounding	1.73E-0.2
GO: 0006952	defense response	3.96E-0.2
	KEGG pathway	**p (Benjamini)**
hsa04060	Cytokine-cytokine receptor interaction	4.65E-03
hsa04660	T cell receptor signaling pathway	2.07E-02
hsa04062	Chemokine signaling pathway	2.97E-02

Conclusion: Early isolated v-lesion has transcriptional profile of immune injury of lower extend compared to T-cell mediated vascular rejection. Early IV may feature non-rejection phenotype and call for reassessment of current Banff histopathology criteria. A larger transcriptome investigation is ongoing to provide insight into cellular phenotypes of AVR after kidney transplantation.

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Clinical Kidney Rejection

BOS464 CX3CL1 IS SIGNIFICANTLY UPREGULATED IN BIOPSIES FROM ACUTELY REJECTING KIDNEY TRANSPLANT RECIPIENTS

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The chemokine CX3CL1 can act as both chemoattractant and adhesion molecule and is expressed on the apical surface of tubular epithelium in human renal transplant biopsy specimens procured during acute rejection (Rej) but also by endothelial and mesangial cells. We studied CX3CL1 on transplant aspiration biopsies (AB) and its evolution post-Rej. First cadaver kidney transplant recipients were studied and divided into three groups: I, stable cases, where AB was done between 7 and 10 days post-transplantation, and which proved Rej-free for at least six months ($n = 42$), group II, Rej cases with AB done the first day of diagnosis (confirmed by a classical Tru-cut biopsy) done concomitantly, and group III post successful treatment of Rej ($n = 5$) all coming from group II, done one week post treatment completion. The AB samples were cytocentrifuged and the CX3CL1 immunostaining was done following APAAP methodology. Neither significant difference was observed by comparing patient demographics nor immunosuppressive treatments. The results are expressed as absolute positive cells (abs), the ratio of positive cells for kidney cells (+/R) and ratio for mononuclear immune cells (+/LM). For group I, abs 10.1 ± 14.4, +/R 0.028 ± 0.046 and +/LM 0.038 ± 0.087; group II, abs 80.7 ± 76.6, +/R 0.22 ± 0.23, +/LM 0.39 ± 0.23; group III, abs 17.6 ± 18.5, +/R 0.024 ± 0.019, +/LM 0.16 ± 0.29. Group I was lower than II, abs ($p = 0.0001$), +/R ($p = 0.0001$), +/LM ($p = 0.0001$). Group II was higher than III, abs ($p = 0.057$), +/R ($p = 0.006$), and +/LM ($p = 0.12$). No differences were observed by comparing I vs. III, respectively for abs, +/R and +/LM, $p = 0.32$, $p = 0.42$ and $p = 0.43$. The negative predictive value for acute rejection recurring to abs < 20 was 97.3% and positive predictive value was 53.8%. We confirm the significant association of CX3CL1 with acute rejection in human kidney transplants and we show for the first time its rapid normalization following successful treatment.

BOS465 C REACTIVE PROTEIN IS MODULATED BY SUBCLINICAL REJECTION IN KIDNEY ALLOGRAFT SURVEILLANCE BIOPSIES

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Clinical and subclinical kidney allograft acute rejection is associated with pro-inflammatory modifications of peripheral blood mononuclear cells, suggesting that renal inflammation contributes to systemic inflammation. Thus, the aim is to evaluate if the presence of subclinical acute rejection in surveillance biopsies at 1 year is related to elevated C reactive protein (CRP) levels.

We analyzed 544 surveillance biopsies performed at 1 year that were classified as normal ($n = 368$), borderline ($n = 148$) or subclinical rejection (SCR) ($n = 28$). CRP levels were divided into quartiles. Patients in 1st, 2nd and 3rd quartile were classified as low CRP ($n = 408$) and patients in the 4th quartile as high CRP ($n = 136$). Univariate analysis showed that the proportion of patients with subclinical rejection was higher in the high CRP group (10.3% vs. 3.4%, $p = 0.0067$). Multivariate analysis showed that independent predictors of high CRP were BMI (Odds ratio (OR) 1.072 and 95% confidence interval (CI) 1.027–1.119) a positive urine culture at the day of the biopsy (OR 2.760 and 95% CI 1.205–6.323) and the presence of subclinical rejection at 1 year surveillance biopsy (OR 7.260 and 95% CI 3.530–14.935).

We conclude that the presence of subclinical acute rejection in stable grafts at 1 year after transplantation is associated with higher CRP levels.

Translational Kidney Rejection

BOS466 CXCL10 EXPRESSION PREDICTS ACUTE T-CELL MEDIATED REJECTION IN HUMAN AND RAT RENAL TRANSPLANTATION

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Background: The gold standard for diagnosis of acute T-cell mediated rejection (ATCMR) following renal transplantation is renal graft biopsy findings. However, the procedure used has various problems, including lack of pathologists with experience in renal graft cases, invasiveness, and sampling error. Thus, a noninvasive general diagnostic method that can be performed quickly is anticipated.
Methods/Materials: We prepared rat allograft and syngeneic graft models of renal transplantation. Chemokine expression was assessed in the rat grafts using quantitative real-time PCR (qRT-PCR). Furthermore, we retrospectively assessed the relationship between pathological findings and chemokine expression using human serum preserved within 14 days of an episode graft biopsy with a cytometric bead array system. The clinical study group consisted of 88 patients who underwent a renal transplant biopsy at Osaka University Hospital between 2008 and 2012.
Results: qRT-PCR results showed that CCL2, CCL3, CCL5, CXCL9, and CXCL10 expressions were significantly increased in the rat allograft model, especially from the early phase after transplantation, in comparison with the syngeneic model (each $p < 0.05$). In humans, as compared to the non-ATCMR cases, those with ATCMR showed significantly higher levels of CXCL9, CXCL10, and CCL5 in serum. ROC curve analysis revealed that serum CXCL10 was best for prediction of ATCMR diagnosis (AUC = 0.89, cut-off value = 180.3 pg/ml).
Conclusions: Serum CXCL10 is a useful biomarker for prediction of ATCMR and may become an important diagnostic tool for determining renal graft rejection.

Clinical Kidney Rejection

BOS467 HOW HARMFUL IS SUBCLINICAL VASCULAR REJECTION?

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Background: Vascular rejection (AVR) has been recognized as a predictor of poor kidney allograft survival exceeding other rejection phenotypes. Because of its severity intensive depletive or antibodies targeting treatment is often used. Evidence describing significance of subclinical AVR is missing.
Methods/Materials: We retrospectively reviewed 1015 patients who underwent kidney transplantation in 2010–2014 to reveal incidence of subclinical AVR in 3-month protocol biopsy of stable allografts. Medical records were analysed to assess effect of therapeutic approach on kidney prognosis.
Results: We identified 19 subclinical AVR in patients receiving kidney transplantation during studied 5-year time period (1.9%). 10 findings fulfilled criteria of isolated v-lesion, while in 5 cases was v-lesion accompanied by tubulointerstitial inflammation. 4 subclinical AVR findings were suspicious of humoral phenotype due to presence of microvascular inflammation but in absence of donor specific antibodies. All patients but one ($n = 18$) received steroids treatment, the remaining patient was not treated. 6-months surveillance biopsy was performed in 10 (55.6%) patients and revealed either normal finding ($n = 8$) or borderline changes ($n = 2$). Renal function remain stable during 2-year follow-up (baseline Cr 126 ± 33 μmol/l, 2-years Cr 129 ± 41 μmol/l, $p = 0.52$). Neither significant increase in proteinuria was observed (baseline 0.3 ± 0.4 g/day, 2-years 0.4 ± 0.8 g/day, $p = 0.3$). 2-years death censored graft survival was 100%.
Conclusion: Subclinical AVR is a rare finding with favourable middle term prognosis for kidney allograft.

Clinical Kidney Histology

BOS468 SENESCENCE AND KIDNEY TRANSPLANT

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Background: Kidney transplant (Tx) outcome is clearly influenced by donor age (DA). Senescence (SCS) could have a key role in graft survival from older donors. Tissue expression of cell-cycle regulator p16INK4a is one hallmark of SCS. The aim of this study was to evaluate p16INK4a in kidney transplant biopsies (Bx) and correlated with graft function, histology, and transplant variables.
Methods/Materials: Retrospective analysis of kidney transplant recipients (KTr) between 2013 and 2014 were included. Donor and recipient age, gender, ischemic time (CIT), mismatch HLA (MMHLA), delay graft function (DGF), immunosuppression, and biopsy proven acute rejection (BPAR) were analysed. Graft function was evaluated with creatinine (Cr) mg%. Immunohistochemistry for p16INK4a was made on paraffin sections with anti-peroxidase (Ventana Benchmark-XT). Univariate and multivariate analysis using Bx with positive p16INK4a as dependent variable were performed. $p < 0.05$ was considered significative.
Results: Sixty two KTr were included. Media DA was 62 year, 31 female. Deceased donor (DD) was 43.5%. Media MM HLA and CIT was 4–5 and 18 h. Eighty percent of DD developed DGF. All patients received induction and triple therapy: prednisone, tacrolimus and mycophenolate. Nuclear staining for p16INK4a was positive in 31/62 early Bx. Other histological findings were: interstitial fibrosis/tubular atrophy in 56.5%, vascular fibrous intimal thickening (CV) in 67%, and microcirculation injury 53% of Bx. BPAR was found in 17 pt. In univariate analysis DA: 48 ± 13 vs. 37 ± 13 years ($p = 0.0008$), donor gender male: 63% vs. 36% ($p = 0.03$) and expanded criteria donor 30 vs. 6% standard criteria ($p = 0.0195$) were significant. Cr was higher at 6 and 12 months post-Tx 1.43 vs. 1.67 ($p = 0.03$) and 1.39 vs. 1.66 ($p = 0.02$). Only CV was significative: 47% vs. 17% ($p = 0.0125$). None variable was significative in multivariate analysis.
Conclusion: SCS cells expressing p16INK4a are more frequent in older donors, with vascular thickening in histology, and poorer graft function.

Clinical Kidney Rejection

BOS469 REJECTION IS A STRONG GRAFT SURVIVAL PREDICTOR IN LIVE DONOR PEDIATRIC RENAL TRANSPLANTATION: 10 YEAR OUTCOME IN A SINGLE MEXICAN CENTER

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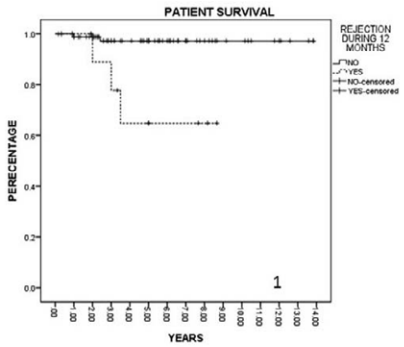
Imss Umae 14 Adolfo Ruiz Cortines, Mexico

Background: Long-term graft function and survival are of particular importance in children assuming they have a longer transplant life span than most adults. Because acute rejection episodes (ARE) continue to be a serious influence on consecutive graft loss, we analysed the effect of ARE on 10 year survival and function in our population.
Methods: Ninety-nine living donor kidney transplant patients (64 male) under 18 years old (13.4 ± 3 years, 3–17 range) were followed with cyclosporine ($n = 82$) and tacrolimus ($n = 17$), mycophenolate mofetil and steroid therapy with Basiliximab induction ($n = 47$) between February 2003 and December 2016.
Results: ARE incidence Patient/graft survival was 97.3/87.5%, 93.2/67% and 93.2/43.2% at 1, 5 and 10 years respectively. Patients who had ARE within 12 months or one ARE during follow-up transplantation had lower 10 year patient survival than those who did not ($p = 0.001$) (Figs 1 and 2). Similarly, patients who had ARE within 12 months or one ARE during follow-up transplantation had lower 10-year graft survival than those who did not ($p = 0.0001$) (Figs 3 and 4). Although induction therapy had better one (95%) and five (68%) year graft survival against those who did not underwent induction (85.9% and 68% respectively), differences were not statistically significant. No differences were noted in patient/graft survival between cyclosporine or tacrolimus use.
Conclusion: ARE is an important risk factor for graft loss in paediatric kidney transplant population. Although it was not statistically significant, antibody induction should be encouraged.



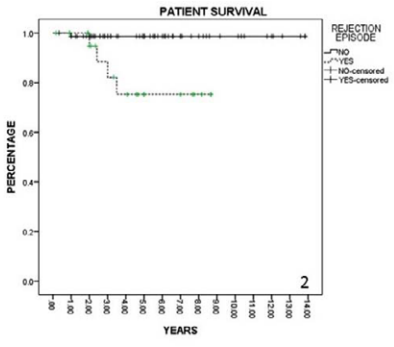
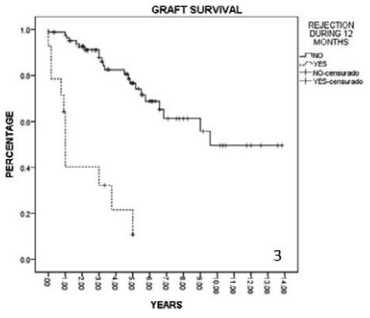


Figure 1. Patient survival in patients who had an ARE during first 12 months after transplant (p< 0.005)
Figure 2. Patient survival in patients who had at least one rejection episode after transplant (p< 0.005)



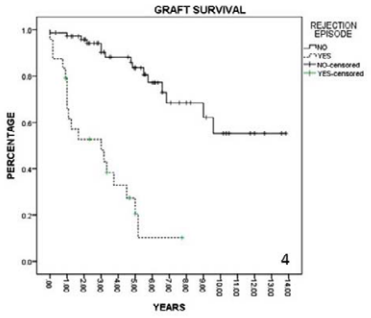


Figure 3. Graft survival differences between patients who had ARE within 12 months after transplant (p<0.005)
Figure 4. Graft survival between patients who had one ARE during follow-up. (p=0.0001)

Clinical Kidney Histology

BOS470 RENAL BIOPSY AS PREDICTIVE TOOL FOR FAILING GRAFTS: A SINGLE CENTER ANALYSIS IN 153 CASES

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Background: The causes of kidney graft loss (GL) are not well understood. Recent papers (El Zoghby2009, Sellarès 2012) suggest immune-mediated damages as leading long term GL causes; when histology is available, a specific GL cause is the most frequent cause.
Methods/materials: 303 renal transplants (RT), performed between 1981 and 2016, failed in the last 5 years (2011–2016); death with functioning graft was the first GL cause (126/303; 37.8%).

In the remaining 194 RT (overall 387 renal biopsies), histological (n = 153) and clinical (n = 18) data were predictive of specific GL causes. DSA were data available in 73%.
Results: Mean graft survival: 10.1 ± 7 years (yrs). 27% failure within 5 years; 28% between 5 and 10 years; 21% between 10 and 15 years; 24% after 15 years.

In 153 RT (78.9%) GL was histologically defined: chronic rejection (CR; 34%), glomerulonephritis (GN; 24%), IF/TA (18%), acute rejection (10%: 9/16 ABMR; 2/16 mixed; 2/16 TCMR; 4/16 "plasmacellularis"), other causes (14%: PVAN, PTLD, diabetic nephropathy, chronic pyelonephritis, CNI toxicity, TMA).

In 18 RT (9.2%) GL was clinically defined (7 vascular; 2 urological; 3 cancer; 4 heart failure; 2 cirrhosis).

In 23 RT (11.8%) the cause of GL was not well defined.

GN ("de novo" + recurrent) are the leading GL cause after 15 years; CR is the first GL cause between 5 and 15 years.

Kidney survival after diagnosis of graft dysfunction was shorter (30.2 ± 33 months) in RT with chronic/active rejection than in RT with GN and non-DSA associated chronic transplant glomerulopathy (55 ± 39 and 58 ± 32 months); p = 0.001
Conclusions: Our data confirm that CR and GN are the leading GL causes in the medium/long term. CNI toxicity is often associated with other histological patterns and is not a leading GL cause in our population, as recent Literature suggest (Matas 2011).

We suggest renal biopsies, also in "end stage" RT, not only to attempt therapies but also to obtain prognostic information in view of the following re-transplantation, pre-emptively or after a period of time on dialysis.

Clinical Kidney Immunology

BOS471 COMPARISON OF THE TREATMENT EFFICACY OF RITUXIMAB AND PLASMAPHERESIS/INTRAVENOUS IMMUNOGLOBULIN COMBINATION WITH HISTORICAL CONTROL IN CHRONIC ANTIBODY MEDIATED REJECTION

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Objective: Chronic antibody mediated rejection (CAMR) is a major therapeutic challenge for achieving long-term graft survival; treatment options are limited to several anti-humoral interventions.
Material and methods: Efficacy of rituximab combination therapy was retrospectively investigated by comparison with a historical control group for allograft function at six month and overall graft survival/dysfunction. The inclusion criterion was biopsy proven chronic AMR according to the Banff 2007 classification. Nineteen patients found eligible, rituximab group had nine patients (rituximab, plasmapheresis and low dose IVIG); control group had ten recipients. Predictive factors for graft failure also investigated according to Banff scores and renal functions.
Results: The comparison of the clinical characteristics and treatment responses is represented in Fig. 1. None of the outcomes were exposed significant efficacy of rituximab, although better treatment response at sixth month (55% vs. 40%, p = 0.51), fewer overall graft failures (33% vs. 60%, p = 0.25) and dysfunctions (66% vs. 80%, p = 0.52). Overall, 47% of patients suffered graft failure. Advanced transplant glomerulopathy was found in 90% of biopsies (all scored ≥2). Peritubular capillaritis score (1.67 ± 0.87 vs. 0.70 ± 0.94, p = 0.04) and interstitial inflammation score (1.78 ± 0.44 vs. 1.00 ± 0.47, p = 0.004) were significantly higher in recipients who suffered graft failure.

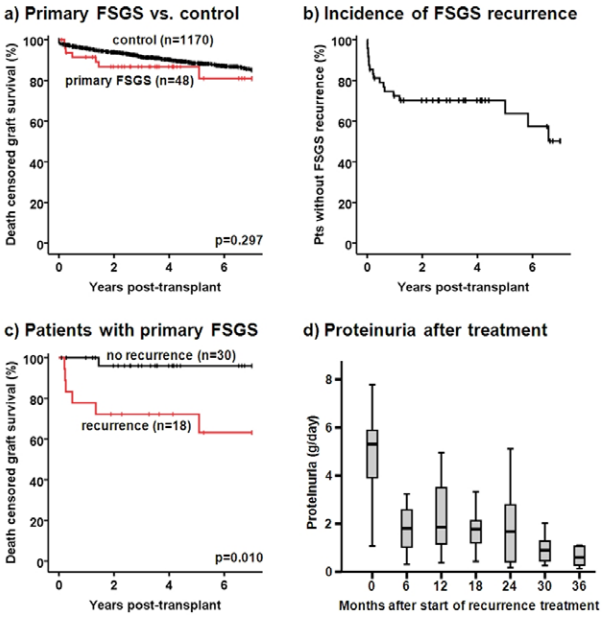
ximab and control group in terms of demographic characteristics, treatment response, allograft functio

	Rituximab Group (n=9)	Control Group (n=10)
e)	78%	80%
	37±12.7	43.1±11.3
e (Living/Deceased)	78%/22%	80%/20%
ween Tx and CAMR (Months)	55.8±51	92.5±63.8
ty at diagnosis	100%	80%
esponse	55%	40%
Dysfunction	66%	80%
	33%	60%
sis (mg/dl)	3.62±3.56	2.99±0.93
osis (ml/min)	30.86±16.74	27.00±13.90
t diagnosis (mg/day)	2246±2259	3924±2334
nth (mg/dl)	3.50±1.88	4.61±2.52
onth (ml/min)	28.33±20.37	19.40±15.10
ixth month (mg/day)	2778±2035	3230±2920
r Estimated aft Survival	62.2%	46.7%

, GFR: Glomerular filtration rate, Tx: Transplantation, CAMR: Chronic antibody mediated rejection

Conclusion: Rituximab could not sufficiently prevent further deterioration of allograft and failed to improve allograft survival in CAMR, especially after settlement of the irreversible transplant glomerulopathy.

Figure 1



Clinical Kidney Rejection

BOS472 LONG-TERM OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH PRIMARY IDIOPATHIC FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

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Introduction: Few data exists analyzing recurrence rates, treatment response and long-term outcomes in kidney transplant recipients (KTR) with primary FSGS.
Methods: This retrospective observational study included 1218 consecutive KTR 2002–2016. All patients with primary idiopathic FSGS were identified applying strict diagnostic criteria. Outcomes were followed over an average of 70.4 months.
Results: We identified 48 KTR (3.9%) with primary FSGS. 7-year death-censored graft survival was 81% (primary FSGS) vs. 85% (control), p = 0.297 (Fig. 1a). Among KTR with primary FSGS, 18 KTR experienced FSGS-recurrence (predicted incidence 50% after 7-years; Fig. 1b). 7-year graft survival in KTR with FSGS-recurrence was significantly worse than in FSGS-KTR without recurrence (63% vs. 96%, p = 0.010; Fig. 1c).

In case of FSGS recurrence a multimodal treatment approach was applied, including: plasma exchange (PE) (100% of patients), cyclosporine i.v. (50%), rituximab (61%) and the "multiple target treatment" according to Canaud et al. (AJT 2009) (39%). The median number of PE-sessions was 27. Proteinuria decreased significantly and persistently during the course of treatment (Fig. 1d). Complete remission of FSGS was observed in 7 patients (39%), another 7 patients (39%) developed partial remission (PE-dependence observed in 4 patients (22%)). 4 patients (22%) with FSGS recurrence experienced early graft loss (< 6 months post-transplant) despite all treatment efforts.
Conclusions: In KTR with primary FSGS a high proportion of recurrences occurred during the long-term follow-up and led to significantly worse graft survival. However, a multimodal treatment approach mostly resulted in resolving of proteinuria and full or partial remission. Graft survival in KTR with underlying primary FSGS was comparable with the control group.

Basic Kidney Immunology

BOS474 PERK-DEPENDENT DEFECTIVE TCR-MEDIATED ACTIVATION OF CD4+ T CELLS IN END-STAGE RENAL DISEASE PATIENTS

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Erasmus Mc, The Netherlands

Introduction: Patients with end-stage renal disease (ESRD) have an impaired immune response with a prematurely aged T-cell system. Mitogen-activated protein kinases including extracellular signal-regulated kinase (ERK) and p38 regulate diverse cellular programs. T cell receptor (TCR)-induced phosphorylation of ERK (pERK) may show an age-associated decline, which can be reversed by inhibiting dual specific phosphatase (DUSP) 6, a cytoplasmic phosphatase with substrate specificity to dephosphorylate pERK. The aim of this study was to assess whether ESRD affects TCR-mediated signaling and explore possibilities for intervening in ESRD-associated defective T-cell mediated immunity.
Methods: PBMCs of ESRD patients ($N = 24$) and age- and cytomegalovirus (CMV)-serostatus matched healthy individuals (HI, $N = 24$) were stimulated with/without CD3/CD28 antibodies and median fluorescence intensity (MFI) of f ERK and p38 phosphorylation was as assessed for different T-cell subsets by flow cytometry. Moreover, inhibition of DUSP6 was evaluated for TCR-induced pERK.
Results: An age-associated decline in TCR-induced pERK-levels was observed in the different CD4+ ($p < 0.05$), but not CD8+, T-cell subsets from healthy individuals (HI). Interestingly, pERK-levels of $CD4^+$ T-cell subsets from young ESRD patients were comparable to elderly patients. pERK-levels in both young as well as old ESRD patients were similar to old HI. A differentiation-associated decline in TCR-induced ERK and p38 phosphorylation was observed, although TCR-induced p38 phosphorylation was not significantly affected by age and/or ESRD. Inhibition of DUSP6 significantly increased TCR-induced pERK-levels of $CD4^+$ T cells in young and elderly ESRD patients, and elderly HI.
Conclusions: TCR-mediated phosphorylation of ERK is affected in young ESRD patients consistent with the concept of premature immunological T cell ageing. Inhibition of DUSP 6 might be a potential intervention enhancing T-cell mediated immunity in ESRD patients.

Translational Kidney Immunology

BOS475 REJECTION OF HUMAN KIDNEY ALLOGRAFTS ACCORDING TO BANFF CLASSIFICATION IS ASSOCIATED WITH A CHEMOKINE-ENRICHED PROTEIN MICROENVIRONMENT IN BIOPSY TISSUE

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Background: Expression profiling efforts of biopsy tissue after kidney transplantation indicate that rejection can be defined by distinct signatures. Based on pathological evaluation (BANFF) as T cell-mediated (TCMR), AMR or borderline rejection, we hypothesized that the presence of immune cells within the graft would be associated with a distinct cytokine milieu. Therefore, we determined the protein microenvironment in kidney biopsies and correlated cytokines and chemokines with pathological staging.
Methods: From our protocol biopsy program, 37 snap-frozen kidney biopsies were obtained from transplant recipients ranging from 2 months to 20 years after Tx with ethical approval, informed consent. Protein lysates of capsule, cortical and medullary biopsy regions were analyzed for 50 cytokines, chemokines using multiplex protein arrays. Histopathological evaluation of was performed according to BANF criteria (14 unsuspicious, 4 TCMR, 5 borderline, 14 AMR).
Results: The protein microenvironment differed significantly between capsular, cortical and medullary kidney regions even in unsuspicious biopsies. In contrast, pro-inflammatory cytokines like IL-6, IL-8 (CXCL8), IFN-g, TNF-a were very low and did not differ between unsuspicious and rejection biopsies. However, significantly higher concentrations of chemokines like CXCL9, CXCL10, CCL5, growth factors, i.e. HGF were detected in cortical and medullary biopsy regions of the rejection group (all $p < 0.01$).
Conclusion: The protein microenvironment of kidney biopsies histologically classified as rejection differs significantly from unsuspicious renal tissue with respect to the chemokine but not the cytokine milieu. Thus, certain chemokines like CXCL9, CXCL10 confirm their qualification as biomarker candidates also at the protein level while typical T cell-derived cytokines seem to perform rather poorly as biomarkers.

Translational Cell Other

BOS476 CHARACTERIZATION OF HUMAN MULTI-CHIMERIC CELLS A NEW TOLERANCE INDUCING CELLULAR THERAPY IN TRANSPLANTATION: A PRELIMINARY STUDY

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University of Illinois at Chicago, United States

Background: Cellular therapies are a promising approach for tolerance induction in solid organ and vascularized composite allotransplantation (VCA) patients that could reduce the negative impact of life-long immunosuppression. We propose a novel cellular therapy of ex vivo created umbilical cord blood – derived multi-chimeric cell (mCC) as an alternative approach to bone marrow based therapies in support of VCA. The aim of this study was to develop the protocol and characterize in vitro the phenotype, genotype and viability of fused human mCC.
Methods: Twelve ex vivo fusions of human umbilical cord blood (UCB) cells were performed. Mononuclear cells (MNC) were isolated from UCB originating from three unrelated donors. Next, MNC were stained separately by PKH26, PKH67 and eFluor670 proliferation dye and fused using polyethylene glycol (PEG). Triple PKH26/PKH67/eFluor670 stained cells were sorted out and subjected to further assessments. Confocal microscopy (CM) and flow cytometry (FC) were used to assess the efficacy of the cell fusion procedure. The distribution of hematopoietic surface markers (CD3, CD4, CD8, CD19, CD45 and CD90) and viability test were performed by flow cytometry. PCR-rSSOP and STR-PCR were assessed to characterize the genotype of mCC.
Results: FC and CM analysis confirmed UCB fusion and creation of human mCC. Using PCR-rSSOP and STR-PCR assays, we determined that human mCC are sharing HLA class I and class II antigens, and other donor specific DNA sequences of all three UCB donors used for fusion. After fusion 90–95% of cells were viable. Phenotype characterization showed expression of all assessed markers on the surface of mCC.
Conclusions: We have successfully confirmed the feasibility of ex vivo fusion procedure and creation of human mCC. We characterized the phenotype, genotype and viability of mCC. This unique concept of mCC introduces a new universal therapy for tolerance induction in solid organ and VCA transplantation.

Basic Kidney Rejection

BOS477 THE SIGNIFICANCE OF URINARY MARKERS IN THE EVALUATION OF GRAFT INJURY IN RENAL TRANSPLANT PATIENTS

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Introduction: Various pathophysiological mechanisms may lead to the graft dysfunction or loss after renal transplantation, such as oxidative stress, ischemia-reperfusion injury and immunosuppressive therapy as well. Early monitoring of tubule damage (*N*-acetyl-b-D-glucosaminidase [NAG], γ-glutamyl transferase [GGT]) as well as the levels of thiobarbituric acid reactive substances (TBARS) in the urine, are possibly an efficient tool to predict the allograft dysfunction. The aim of this study was to determine the levels of TBARS, as well as the activity of ectoenzymes (NAG, GGT) in the urine of transplanted patients. Secondly, we wanted to estimate whether or not, tacrolimus daily dose [TDD] might have affected oxidative or tubular injury.
Materials and methods: The study included 72 patients who were on tacrolimus (TAC) based immunosuppression and 62 healthy individuals, who did not differ in terms of age and gender structure. We measured the urinary TBARS levels in order to evaluate oxidative injury, as well as the activities of ectoenzymes (NAG, GGT) in urine and plasma to evaluate tubular damage.
Results: The level of urine TBARS and NAG activity in urine and NAG activity in plasma were significantly higher in patients compared to controls, whereas there was no difference in GGT activity in urine and plasma of both examined groups. The levels of urine TBARS showed a significant positive correlation with the levels of urine NAG and eGFR. Additionally, there was no significant correlation between TBARS, NAG and GGT in the urine of the patients and TDD.
Conclusion: Patients after kidney transplantation experience higher oxidative stress, and possibly greater tubular injury compared to healthy individuals. That implicates that oxidative stress could be one of the causes of the tubular damage in transplanted patients. Tacrolimus may probably exert nephrotoxicity, but our study showed this effect is independent from oxidative stress mediated reduction in renal function.

BOS478 EPITOPE BASED HLA MATCHING BY USING ANTIBODY REACTIVITY WITH HIGH RESOLUTION ALLELE TYPING AND HLAMATCHMAKER ALGORITHM BASED SOFTWARE

Sedat Tanju Karadeniz[1], Sabahat Akgul[2], Hayriye Senturk Ciftci[2], Yeliz Ogret[2], Fatma Oguz[2], Kemal Yelekci[3], Filiz Aydin[2]

[1]Istanbul Bilim University Florence Nightingale Hospital, Turkey; [2]Istanbul University, Istanbul Medical Faculty, Turkey; [3]Kadir Has University, Turkey

Background: The donor specific antibodies are most important barrier to successful kidney transplantation. By using the solid phase antibody detection assay with single HLA alleles with bead-array technology has increased the sensitivity and accuracy for the detection of HLA antibodies. These antibodies are the immune response of mismatched HLAs, which can occur after pregnancy for women, blood transfusions, and previous transplantation. But, some allosensitized patients have no detectable DSAs before transplantation in their serum. These patients are at elevated risk for antibody mediated rejection occurring in the immediate post transplantation period.
Methods/Materials: The determination of epitope-specific antibodies in sensitized patients has an important improvement for organ transplantation. Evaluating the degree of epitope based HLA compatibility would be more meaningful rather than HLA antigens. An epitope analysis of serum antibody reactivity for sensitized patients would be fortunate by identifying of permissible HLA antigens on the waiting list for kidney transplantation. The HLAMatchmaker algorithm developed in the Acceptable Mismatch Program to identify donors for highly sensitized patients and has already demonstrated reduced waiting time and better graft survivals.
Results: By using the computer analysis software based on HLAMatchmaker algorithm, determination of epitope-specific antibody from serum reactivity pattern with single antigen assay greatly enhances of post transplantation production of DSAs against antigens.
Conclusion: Even if the patient had very low level or negative DSA in pre-transplantation sera, the post-transplantation antibody response for a specific epitope shared by previous immunizer could induce antibody-mediated rejection.

Basic Kidney Immunology

BOS479 THE ROLE OF SOLUBLE CTLA-4 AS A NON-INVASIVE BIOMARKER FOR DIAGNOSIS OF KIDNEY ALLOGRAFT REJECTION: A PRELIMINARY STUDY

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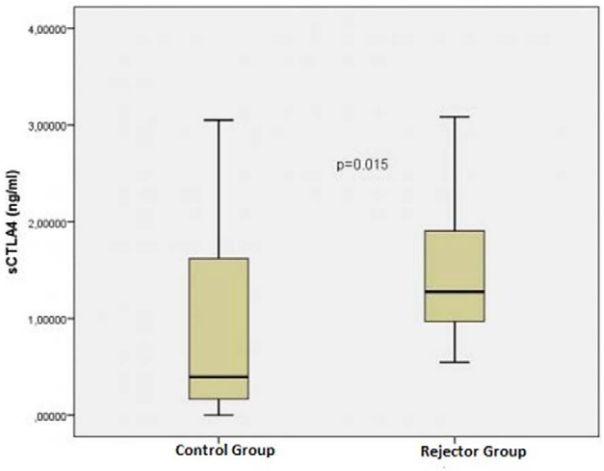
[1]Haydarpaşa Numune Research and Training Hospital, Transplantation Center, Turkey; [2]Department of Medical Genetics, Marmara University Faculty of Medicine, Turkey; [3]Department of General Surgery, Namık Kemal University Faculty of Medicine, Turkey

Background: Cytotoxic T-lymphocyte antigen 4 (CTLA-4) is a cell surface protein, which plays a central role in the CTLA-4/CD28/CD80/86 co-stimulatory pathway. CTLA-4 have two isoforms, flCTLA-4 (full length, exon 1–4) responsible for main function, however, other isoform sCTLA-4 (soluble, exon 1, 2 and 4) thought to be competitively inhibits the flCTLA-4 and responsible for activation of the immune response. In the present study, we investigated the rationale for use of the serum sCTLA-4 as a non-invasive biomarker for diagnosis of allograft rejection.
Methods: Two groups were formed; rejectors group consist of 24 patients who had diagnosis of biopsy-proven acute cellular or acute/chronic antibody-mediated rejection, control group consisted of 16 kidney transplant recipients without any clinical or laboratory allograft dysfunction. Human CTLA-4 enzyme-linked immunosorbent assay (ELISA) was used for the quantitative detection of serum sCTLA-4 (BMS276, eBioscience San Diego CA). The local ethical committee approved the study. Mann-Whitney U test was used for statistical evaluation.
Results: The rejectors group (24 patient, 15 Male/ 9 Female) and control group (16 patient, 11 Male/7 Female) did not show any significant difference in terms of age (43.5 ± 10.4 vs. 48.2 ± 9.5 years, p = 0.16), donor source (living donor 79% vs. 69%, p = 0.37) and induction immunosuppressive therapy (Anti-Thymocyte Globulin 46% vs. 31%, Basiliximab 21% vs. 44%, p = 0.22). In the rejectors group, there were three acute antibody mediated rejections, four acute cellular rejections and 17 chronic antibody-mediated rejections. Rejectors group had significantly higher serum sCTLA-4 levels than the control group (1.49 ± 0.75 ng/ml vs. 0.94 ± 1.07 ng/ml, p = 0.015) (Figure).
Conclusion: In this preliminary study, we found that; the quantitative measurement of serum sCTLA-4 levels, have the potential for to be a non-invasive biomarker for prediction of the allograft rejection.



The comparison of the sCTLA-4 levels in Allograft Rejectors and Control groups

Basic Heart Immunology

BOS480 WHICH TR1 IS BETTER FOR TRANSPLANT TOLERANCE INDUCTION: COMPARING THE TR1 GENERATED BY IL-27 OR TGF-βPLUS IL-27

Guangxiang Gu, Qiang Xia
Shanghai Jiaotong University, China

IL-10 producing T cells (Tr1) are important for the transplant tolerance induction. However, Tr1 can be induced in two methods: IL-27 or TGF-βplus IL-27. We still do not know which one is better for transplant tolerance induction. First, we generated foxp3-GFP IL-10-Thy1.1 mice, sorted Foxp3- naïve T cells, and differentiated into Tr1 by IL-27 OR TGF-βplus IL-27. We found no difference on IL-10 expression between the two groups. However, RNA-seq showed that Tr1 generated by IL-27 expressed more pathogenic genes, such as IL-23R, but less tolerant genes, such as prdm1, irf1, Tim-3, Batf. When co-cultured with effector T cells, we found that Tr1 generated by TGF-βplus IL-27 could better inhibit the T cell proliferation. Further, we adoptively transferred the Tr1 into allogeneic heart transplant mice (intravenously) to induce tolerance, and found that both Tr1 could prolong the graft survival, but the graft in TGF-βplus IL-27 group could survive longer than the other one, and the graft infiltrating T cells express less IFN-g, but more IL-10. At last, we found that the two kinds of Tr1 were much similar by RNA-seq when generated from IL-23R ko T cells, suggesting the function of Tr1 generated by TGF-βplus IL-27 may be dependent on IL-23R. In summary, the Tr1 generated by TGF-βplus IL-27 is better than that generated by IL-27 for transplant tolerance induction.

Basic Cell Immunology

BOS481 GMSCS PROTECT ACUTE-GVHD BY SUPPRESSING EXPANSION AND KILLING OF EFFECTOR CD8+ CELLS THROUGH CD39/ADENOSINE A1R AND A2BR PATHWAYS

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[1]The First Affiliated Hospital of Nanjing Medical University, China; [2]Nanjing Medical University, China

Background: Human gingival tissue-derived MSCs (GMSCs) have been identified as an important treating strategies for cell therapies particularly in autoimmune disease recently. However there is no report for GMSCs in acute-GVHD.
Aim: To investigate the role of GMSCs in treating acute-GVHD and the underling mechanisms of GMSCs in regulating autoimmune disease.
Method: Two different models have been used to test the effect of GMSCs in treating acute-GVHD. The expansion and survival of donor and host cells in vivo were tested by flow cytometry. CD4 and CD8 T cells were co-cultured with GMSCs with the addition of IL-2 and TGF-β to test the effect of GMSCs in regulatory T cells generating in vitro. In some experiment, CD39 inhibitor (POM1) and Adenosine receptor A1, A2A, A2B, A3 inhibitors were used to estimate the mechanism of GMSCs in treating acute-GVHD.
Result: GMSCs infusion markedly suppressed the engraftment of donor CD8+ cells, the expression of Granzyme A and B, the cytotoxic effect of donor CD8+ cells and the production of T cell cytokines in acute-GVHD. Our result showed that GMSCs have strong ability in treating acute-GVHD and increase survival. Meanwhile the inhibition of GMSCs is dependent on CD39 signaling. Adenosine receptor A1 and A2B are partly involved in GMSCs induced acute-GVHD protection.
Conclusion: We suggest that therapeutic approaches to treat acute-GVHD can be effective by using GMSCs.

Basic Liver Rejection

BOS482 IDENTIFICATION OF A STABLE GENE SIGNATURE OF TRANSPLANT TOLERANCE TO LIVER ALLOGRAFT BY META-ANALYSIS

Guangxiang Gu, Qiang Xia
Shanghai Jiaotong University, China

Transplant tolerant to a liver graft display a specific blood cell transcriptional pattern but results from six different studies were not consistent, raising the question of relevance for future clinical application. To resolve this, we sought to identify a common gene signature, specific functional and cellular components, and discriminating biomarkers for tolerance following liver transplantation. A meta-analysis of studies identified a robust gene signature involving CD4 T cell and B cell function. Experimental validation was performed on new tolerant samples and using a selection of the top-10 biomarkers. Beyond the confirmation of T cell and B-cell involvement, our data also indicated participation of other cell subsets in tolerance. Furthermore, we identified 12 new biomarkers. Thus, the use of the top 10 biomarkers may provide a common and standardized tool towards personalized medicine for the monitoring of tolerant patients among liver allotransplant recipients. These data may contribute to a better understanding of tolerance maintenance mechanisms.

Basic Pancreas/Islet Rejection

BOS483 EFFECT OF PRO-SENESCENT ENDOTHELIAL MICROPARTICLES ON RAT PANCREATIC ISLETS: IMPACT FOR TRANSPLANTATION

Mohamad Kassem[1], Guillaume Kreutter[1], Ali El Habhab[1], Philippe Baltzinger[1], Lamia Amoura[1], Malak Abbas[2], Blandine Yver[1], Valérie Schini-Kerth[2], Florence Toti[2], Laurence Kessler[1]

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Aging is one of the limiting causes of graft dysfunction. Pancreatic islets transplantation by portal vein infusion is a cell therapy for patients with brittle type 1 diabetes. Microparticles (MPs) are submicron plasma membrane vesicles shed by stressed or apoptotic cells and circulating in blood. We investigated whether pro-senescent endothelial MPs (PS-EMPs) prompt islet senescence and dysfunction in vitro.

Islets were isolated from male Wistar rats (200–250 g $n = 5$). MPs were isolated from primary porcine coronary artery endothelial cells (ECs) after the first (P1) or the third passage (P3). Pancreatic islets were treated for 24 h with 5 nM washed MPs from P1 young and P3 senescent cells or by 100 μM H_2O_2. Viability was assessed by fluorescence microscopy (Propidium iodide/ Fluorescein diacetate double labeling), apoptosis by flow cytometry (PI /Annexin V labeling). Islet function was assessed by insulin secretion measured in high compared to low glucose medium (25 vs. 2.5 mM). Senescence markers p53, p21 and p16 were assessed by western blot, integration of MPs stained by PKH26, a lipid fluorescent probe, analyzed by microscopy and flow cytometry.

The ability of islets to secrete insulin in response to glucose elevation significantly decreased in the presence of P3 ECs-derived MPs (1.7 ± 0.2 vs. 2.7 ± 0.2 P3 MPs- vs. – UN (untreated islet), $p < 0.05$), without altering islet viability (89% $\pm$ 1.7 vs. 93% $\pm$ 1, MPs- vs. -UN) and with no evidence of apoptosis. P3 MPs induced a significant 2 fold increase of p53, p21 and p16 expression ($p < 0.05$), whereas P1 MPs had no effect. Microscopy and flow cytometry showed an important MP incorporation in islets after 24 h.

PS-EMPs induce cellular senescence in islets and alter their function. These data suggest an impact of the islet donor age on graft success and question the relevance of graft pre-conditioning to preserve ECs and limit the generation of pro-senescent MPs in the isolated islets suspension prior transplantation.

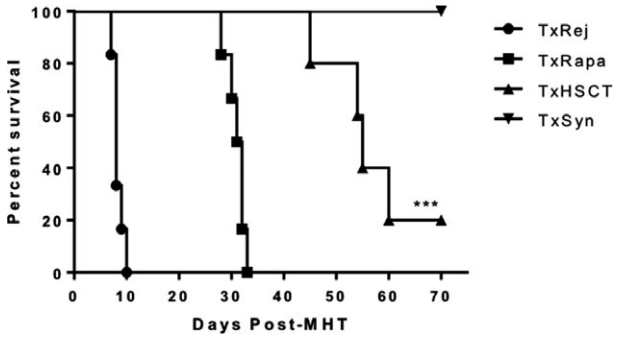
Basic Heart Immunology

BOS484 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION INDUCES TOLERANCE OF FULLY MISMATCHED MURINE HEART ALLOGRAFTS

Andrzej Chruscinski[1], Hassan Sadozai[1], Vanessa Rojas-Luengas[1], Kaveh Farrokhi[1], Wei He[1], Jianhua Zhang[1], Dario Ferri[1], Oyedele Adeyi[1], Reginald Gorczynski[1], Nazia Selzner[1], Handy Yowanto[2], Jane Luo[2], Jeff Chapman[2], David Grant[1], Harold Atkins[3], Gary Levy[1]

[1]University Health Network, Canada; [2]Sciex, United States; [3]Ottawa Hospital Research Institute, Canada

Background: The establishment of immune tolerance would eliminate the need for long term immunosuppression which negatively impacts long term survival and quality of life of solid organ transplant recipients. Autologous hematopoietic stem cell transplantation (HSCT) has been shown recently to re-establish tolerance in patients with autoimmune disease.
Methods: We investigated if HSCT can promote tolerance in the setting of allotransplantation. Total body irradiation (13 Gy) followed by HSCT from C57Bl/6 marrow donors was performed one-week following heterotopic transplantation of fully H-2 mismatched BALB/c cardiac allografts into C57BL/6 recipient mice. HSCT recipients were treated with rapamycin (2 mg/kg/day) for 14 days starting 1 day prior to HSCT to prevent early acute cellular rejection and to promote regulatory T cell expansion. Parallel control groups, with or without rapamycin, did not undergo HSCT. Graft function was assessed daily by manual palpation and grafts that continued to beat ≥70 days following HSCT were considered to be tolerant.
Results: Without HSCT, cardiac allografts were rejected within 14 days whether or not the recipients received rapamycin. Cardiac allografts in mice that underwent HSCT had prolonged survival (tolerance) (Figure). HSCT recipients had a primary response to donor antigens in a one way mixed lymphocyte reaction; markedly diminished donor specific antibody levels; did not develop autoantibodies; and had significantly higher frequencies of peripheral and intra-graft CD25+ FOXP3+ Treg consistent with development of peripheral immunological tolerance to the cardiac allograft.
Conclusion: These data provide compelling evidence for the ability of HSCT to re-educate the immune system in the setting of allogeneic solid organ transplantation, leading to tolerance induction. This provides support for the clinical testing of HSCT to induce tolerance in organ allograft recipients.



Basic Others Immunology

BOS485 LOW-DOSE TACROLIMUS SUPPORTS T CELL REGULATION IN A MOUSE SKIN TRANSPLANT MODEL

Paloma Riquelme, Anja Kammler, Hans Schlitt, Edward Geissler, James Hutchinson

University Hospital Regensburg, Germany

Background: The contribution of T cell-mediated regulation to long-term stable immunosuppression after solid organ transplantation is not yet fully appreciated. Low-dose tacrolimus (Tac) permits a level of Treg function, which might reduce the need for generalised immunosuppression, whereas higher Tac doses inhibit Tregs. A better understanding of the balance between effector responses, regulation and immunosuppression could lead to safe Tac minimization strategies and optimized graft survival.
Methods/Materials: Tac delivery in food pellets was established using a BALB/c-to-C57BL/6 skin transplant model: high-dose (150 mg/kg food, indefinite graft survival); mid-dose (100 mg/kg food, prolongs graft survival); low-dose (75 mg/kg food, no effect). Low-dose Tac was combined with a weak regulation-inducing protocol (αCD154 + DST).
Results: αCD154 + DST prolonged graft survival from 8.3 ± 0.42 to 39.4 ± 5.8 days. Combining αCD154 + DST with low-dose, sub-therapeutic Tac had a synergistic effect (74.4 ± 4.1 days). In this model, Treg-mediated prolongation of graft survival was a graft-intrinsic phenomenon that depended upon as few as 5000 intragraft Tregs. Rejection in this model occurred after d50 when $CD8^+$ T cells accumulated in dLN. On d50, the balance between effector and regulatory responses was investigated by: 1) enhancing effector responses by adoptive transfer of T cells (62.4 ± 2.0 days); (2) disrupting Treg activity with αGITR (69 ± 5.6 days), αPD-L1 (65.9 ± 2.6 days), αTGFβ (69 ± 1.4 days) or DTR-depletion of $Foxp3^+$ cells (58.8 ± 0.1 days); or 3) by interrupting Tac therapy (61.4 ± 1.5 days). Graft loss after Tac withdrawal on d50 could be delayed or prevented by boosting regulatory responses with αCD154 + DST or Treg-promoting interventions.
Conclusion: This study shows that low-dose tacrolimus favours regulation-dependent allograft survival in a fully-mismatched mouse skin transplant model by preferentially suppressing effector T cells, hence stabilizing the balance between effector and regulatory responses.

Basic Cell Other

BOS486 TOWARDS PERSONALISED REGENERATIVE MEDICINE: MUTATIONS IN HUMAN INDUCED PLURIPOTENT STEM CELLS

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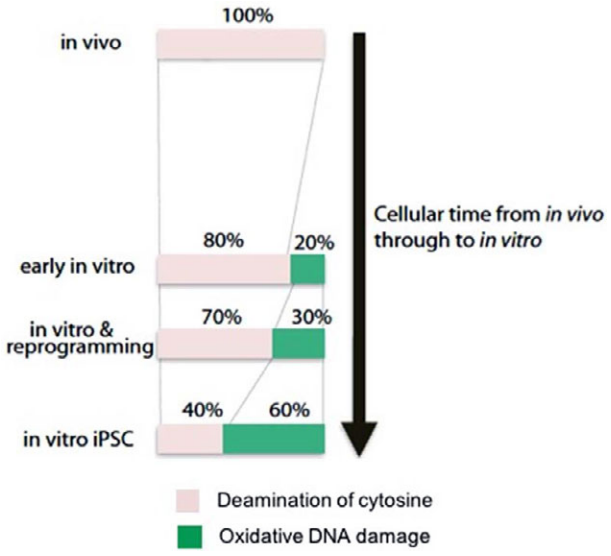
[1]Department of Surgery, University of Cambridge, Cambridge, United Kingdom; [2]Wellcome Trust Sanger Institute, United Kingdom

Background: Reprogramming involves the overexpression of pluripotency genes in somatic cells to produce pluripotent cells similar to embryonic stem cells. These induced pluripotent stem cells (iPSCs) have the potential to revolutionise clinical medicine through the development of personalised cell based therapies as an alternative to whole organ transplantation. However a



major safety consideration is the mutations identified in iPSCs which represent a barrier to clinical translation. The nature and importantly the source of these mutations remains unclear, whether they are somatic in origin or accrued through reprogramming.
Materials and methods: Somatic cells were derived from skin and blood of healthy subjects and reprogrammed into iPSCs using retroviruses. Exome and whole genome DNA sequencing was performed which enabled clonal and sub-clonal mutations to be characterised and mutational signatures to be identified.
Results: Genomic profiling of the iPSCs revealed genetically stable lines with relatively few mutations, termed single nucleotide variants (SNVs) which were dispersed evenly across the genome and none found to be driver mutations in oncogenes. By sequencing the genomes of polyclonal and monoclonal somatic cells and derived iPSCs, it was possible to identify mutations generated in vivo, those generated during reprogramming and finally those during expansion of iPSCs in cell culture. Somatic cells had a mutation rate in vitro of 14 SNVs per cell per generation whilst iPSCs exhibited a ten-fold lower rate. Furthermore analyses of mutational signatures suggested that deamination of methylated cytosine may be the major mutagenic source in vivo, whilst oxidative DNA damage becomes dominant in vitro.

Conclusions: Reprogramming appears to be mutagenic at the nucleotide resolution but the mutation rates of in vitro cultured iPSCs appears to be reassuringly low. Further understanding of the genetic stability of iPSCs will inform future clinical therapies

Clinical Kidney Donation and Donor Types

BOS487 OUTCOME OF PATIENTS AFTER KIDNEY TRANSPLANTATION (KTX) WITH DCD-GRAFTS (DONATION AFTER CARDIAC DEATH) IN GRAZ

Silvia Schaffellner[1], Sabine Zitta[2], Estrella Jakoby[1], Astrid Mauric[2], Katharina Artinger[2], Michael Sereinigg[1], Alexander Kirsch[2], Philipp Stiegler[1], Helmut Mueller[1], Daniela Kniepeiss[1], Peter Schemmer[1], Alexander Rosenkranz[2]
[1]Medical University Graz Clinical Department of Transplantation Surgery, Austria; [2]Division of Nephrology, Department of Internal Medicine, Medical University of Graz, Austria

The ubiquitous shortage of donor organs in Europe necessitates the supplementary acceptance of donation after cardiac death (DCD) donors in addition to brain death donors (DBD) in the Eurotransplant (ET) zone. In DCD donors, the so-called "no touch period" after cardiac arrest – which is defined by law and the local protocol – can lead to ischemia with consecutive organ impairment. In this retrospective analysis, "delayed graft function" (DGF) of DCD-donors organs after kidney transplantation was evaluated.

10 DCD kidney donations were accepted and retrospectively evaluated from 2013 to 2016. The grafts from this Non Heart-Beating Donors (NHBD) were harvested according to the group 3 of the Maastricht-Criteria. Patients from group 3 are nursed under intensive care and their death is considered to occur in foreseeable future. This allows donor logistics to be organized properly based on defined protocols. Criteria of organ acceptance are donor age below 65 years, no relevant comorbidities and an cold ischemia time below 20 h. Immunological high risk patients were declined.

The average (av.) donor age was 54 years with a standard deviation of 23. The av. no touch period was 15 min (10–20). The av. overall ischemia time was 17 h (14–23) and av. operation time 155 min (120–190). 5 donors were male and 5 recipients women. The av. recipient age was 59 years (45–68). 6 (60%) patients suffered from DGF with an av. time of dialyses of 11 days (1–28). Basiliximab was used as an induction therapy in 6 patients and ATG was used in 4 patients. 4 patients with DGF received ATG. During the observation period, 1 rejection (BANFIII) was documented. To date, 9 of the 10 included patients have good kidney function, with av. serum-creatinine of 1.6 mg/dl, av. GFR of 48 ml/min. 1 patient died.

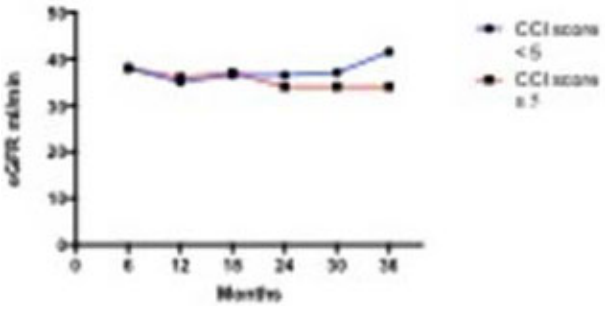
Acceptance of DCD-grafts significantly increases the organ pool. In the literature DGF occurs in 69% of DCD and 29% in DBD-recipients. However, the expected higher amount of DGF has been certified also in this small cohort.

BOS488 IMPACT OF COMORBIDITY ON OUTCOMES IN OLDER PATIENTS UNDERGOING KIDNEY TRANSPLANTATION

Ummul Contractor, Usman Khalid, Paola Donato, Tarique Sabah, Laszlo Szabo, Mohamed Ilham, Argiris Asderakis
Cardiff Transplant Unit, University Hospital of Wales, United Kingdom

Background: Kidney transplantation has increased among older patients. Our unit has achieved excellent results using old DCD donor kidneys into older recipients. The Charlson Comorbidity Index (CCI) has been shown to be a sensitive tool predicting mortality in those with comorbid conditions. We aimed to assess if we could use CCI as a prognostic tool to aid selection of older candidates, based on graft function and patient and graft survival.
Methods: We investigated a cohort of elderly (age >60) kidney transplant patients; all receiving kidneys from older DCD donors (age >60) who had follow up of 3 years. Sixty two patients were identified, and CCI was calculated for each patient based on comorbidities at the time of surgery. Pearson correlation was used initially to correlate graft function (eGFR) with CCI. Given the confounding factors we additionally compared the patient and graft survival and function at 1 and 3 years between patients having a CCI<5 compared to those with CCI ³5.
Results: The CCI score ranged between 2 and 10. Using Pearson-correlation there was no significant correlation of CCI with graft function (eGFR) at 1 year ($R^2 = -0.14$, p = 0.28) or 2 years ($R^2 = -0.19$, p = 0.15). Patient survival at 1 and 3 years was 94% and 90% among those with CCI less than 5, compared to 90% and 76% respectively in those with CCI ³5. Graft survival at 3 years (censored for death) was 97% in patients with CCI less than 5 vs. 90% in those with higher CCI. A graph with the respective eGFRs of the two groups is presented below.

Conclusion: In our cohort, patients with higher CCI had higher mortality at 3 years and slightly lower graft survival and graft function (not statistically significant). Given the small number of patients in this cohort, future studies with a larger cohort are needed to confirm these findings.



Clinical Kidney Allocation

BOS490 INCREASING ACCESS TO KIDNEY TRANSPLANTATION OF HIGHLY SENSITIZED PATIENTS BY AN ORGAN EXCHANGE PROGRAMME BASED ON VIRTUAL CROSSMATCH IN ANDALUSIA. ANDALUSIAN WORK GROUP FOR HIGHLY-SENSITIZED PATIENTS

Antonia Alvarez[1], Auxiliadora Mazuecos Blanca[2], Abelardo Caballero González[3], Mercedes Cabello Díaz[4], Teresa García Álvarez[2], Antonio Garrido Torres-Puchol[5], Miguel Ángel Gentil Govantes[6], María Francisca González Escribano[7], Rafael González Fernandez[8], Jesús Huet Ruiz-Matas[1], Antonio Nieto Díaz[9], Manuel Osorio Moratalla[10], Alberto Rodriguez Benot[11], Manuel Alonso Gil[1]

[1]Regional Transplant Organisation of Andalusia, Spain; [2]Nephrology Department, Hospital Puerta Del Mar, Cádiz, Spain; [3]Immunology Department, Hospital Regional De Malaga, Malaga, Spain; [4]Nephrology Department, Hospital Regional De Malaga, Malaga, Spain; [5]Immunology Department, Hospital Virgen De Las Nieves, Granada, Spain; [6]Nephrology Department, Hospital Virgen Del Rocio, Sevilla, Spain; [7]Immunology Department, Hospital Virgen Del Rocio, Sevilla, Spain; [8]Immunology Department, Hospital Reina Sofia, Cordoba, Spain, Spain; [9]Immunology Department, Hospital Puerta Del Mar, Cadiz, Spain; [10]Nephrology Department, Hospital Virgen De Las Nieves, Granada, Spain; [11]Nephrology Department, Hospital Reina Sofia, Cordoba, Spain

Introduction: Anti-HLA antibodies reduce opportunities of kidney transplantation for patients on waiting list.
Objectives: We describe the results of a kidney allocation system for highly-sensitized (HS) patients, based on Virtual-Crossmatch (VCM) and Calculated-PRA implemented in Andalusia (a region in southern Spain with a population of 8.4 million inhabitants) and comprising five andalusian kidney transplant centres.
Method: The VCM-Programme started in June 2012. A specific computer program was designed to perform an on line VCM after introducing donor HLA antigens and patients' anti-HLA antibodies. Only patients with PRA $\geq$ 95% determined by Luminex© assay in two consecutive studies were included.

When a potential donor fulfils criteria, immunology laboratory performs the VCM. The software provides a list of possible candidates arranged by blood type and date of onset of dialysis, and applies criteria in case of more than one candidate. A negative crossmatch by CDC is mandatory before transplantation.
Results: 205 HS-patients with median time on waiting list of 5.1 years (1–23.5 years) were included during the first 57 months of the VCM-Programme. During this period, 1915 deceased kidney transplants were performed in Andalusia, 72 in HS-patients (3.7%). After being included in VCM-Program, kidney transplantation in HS-patients was performed at a median time of 261 days (1–1681 days).

Compared with our previous kidney exchange program based on sera exchange and CDC crossmatch: 1165 deceased kidney transplants were performed in Andalusia during 44 months, 12 in HS-patients (1%), which means one transplant every 144 days, while with VCM-Program, 72 of 1915 cadaveric kidney transplants (3.7%) were performed in HS-patients ($p = 0.0048$), one transplant every 23.7 days. This new system also reduces the number of positive crossmatches with a predictive negative value of 91.3%.
Conclusions: Kidney allocation based on VCM significantly increases access to kidney transplantation for HS-patients

Clinical Kidney Donation and Donor Types

BOS491 HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY (HALDN): CAN WE ANTICIPATE TECHNICAL DIFFICULTY?

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Catholic University of the Sacred Heart Renal Transplant Unit, Italy

Background: Hand assisted laparoscopic donor nephrectomy (HALDN) is spreading rapidly. Our aim was to identify the potentially most challenging cases by pre/intra operative assessment.
Material and methods: Demographic data (gender, age, BMI) and CT scan parameters such as donor renal artery length and arterial and venous multiplicity/anomalies were analyzed. All operations were performed by the same surgeon and graded on a scale of 1–4 for technical difficulty (*easy*, *moderately difficult*, *difficult*, *very difficult*) based on: mobilization of colon, kidney, dissection of renal artery (RA), renal vein (V), ureter, division of adrenal vein, availability of laparoscopic space.

Results : A total of 88 HALDN, 11 right and 77 left were studied. Mean age was 51 years, mean BMI 25 kg/m^2. Multiplicity of arteries was observed in 24/88 (27.2%) patients. Only 2/59 (3.3%) left kidneys with a short single RA (11 mm and 14 mm respectively) resulted in multiple arteries at implantation, in one case the smaller branch was tied with good graft outcome. In the other, a perigraft hematoma occured, successfully drained. In 21/88 (23.8%) cases the operation was graded *difficult* or *very difficult*. In 3 cases the operation was *very difficult* due to hard perirenal scarring/fibrosis (2 cases), excessive perirenal fat (1 case). Difficulty was significantly influenced by BMI ($p = 0.0001$) and male sex ($p = 0.003$) and considering these two parameters together $R^2 = 0.415$ ($p < 0.01$). Overall, recipient and graft survival were both 100%, 2 recipients of elderly donor kidneys experienced DGF (2.2%).
Conclusions : Even in the most challenging cases HALDN proves to be an extremely safe technique. High BMI and male sex seem to be predictive of technical difficulty, that is not influenced by arterial multiplicity. With the currently available laparoscopic stapling devices RA length >14 mm is unlikely to result in multiple arteries. The development of new and narrower staplers might further decrease the occurrence of this event.

Basic Kidney Donation and Donor Types

BOS492 LONG TERM EVALUATION OF LIVING KIDNEY DONORS: EIGHT YEARS POST DONATION

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[1]Urology and Nephrology Center Mansoura University Egypt, Egypt; [2]Faculty of Medicine, Zagazig University, Egypt; [3]Urology and Nephrology Center, Mansoura University, Egypt

Background: Kidney transplantation particularly from a living donor is the treatment of choice for most patients with end stage renal disease. The shortage of deceased donor kidneys and the superior results achieved with living donor kidney transplantation made it the most preferable worldwide. Safety of the donor is a critical issue and the process of donation should be stopped if any doubt on donor safety arises.
Methods: The transplant registry system at Mansoura Urology & Nephrology Centre was reviewed to assess the safety of Eighty- one donors who donated their kidneys between December 2007 and November 2008 using both univariate and multivariate analysis. Their evaluation was done via clinical, laboratory and radiological assessments which were carried out basally pre-donation, 3, 6, 12 months and then annually till 8 years post donation.
Results: The mean age at time of donation was 37.7 $\pm$ 9.8 years ranging from 22 to 64 years and the majority were females (61, 75.3%). Right nephrectomy was carried out in 40 donors. The mean BMI increased significantly post donation. Blood pressure showed mild increase from the basal values as mean systolic blood pressure increased by 5 mmHg and mean diastolic blood pressure increased by 2 mmHg and only six donors developed post donation hypertension. The mean serum creatinine levels increased significantly in the first three months post donation. Later, there was a significant improvement till the end of the study period. Although GFR showed significant reduction in the early post donation period, later on it increased to near 70% of the basal values. Proteinuria increased with follow up but still appears to be of no clinical significance. Two donors showed ECG changes of LVH and 2 other showed changes of ischemic heart disease.
Conclusion: Living kidney donation is a safe procedure which carries a minimal risk in comparison with the benefits that will be gained for the transplant recipients.

Clinical Kidney Other

BOS493 CONTINUOUS INFUSION OF LOCAL ANESTHESIA AFTER HAND-ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY

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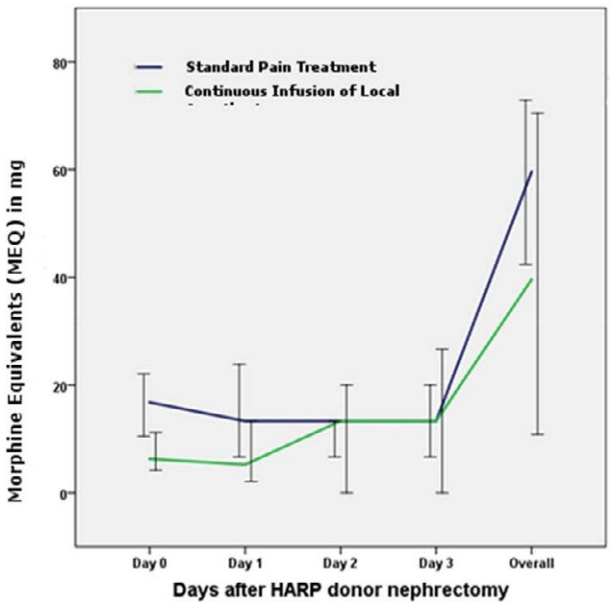
Introduction: Postoperative pain management determines donor comfort after living kidney donor nephrectomy. Opioid based pain treatment due to the



WHO-pain ladder represents the standard of care. This standard pain treatment (SPT) is often limited due to side effects. Continuous infusion of local anesthesia (CILA) is an alternative, which treats the pain directly at the place of its origin. The aim of this study wants to evaluate, if CILA could reduce the dose of opioids after hand-assisted retroperitoneoscopic donor nephrectomy (HARP).
Methods: 15 living donors operated with the HARP technique were treated with SPT and compared to the following 15 donors treated with CILA. The difference in morphine equivalents (MEQ) was the primary outcome parameter.
Results: On the day of the donor nephrectomy (day 0) and the following day (day 1) HARP donors with CILA received less opioids compared to SPT-group (MEQ day 0: 6.3 mg, IR 4.2–11.2 vs. 16.8 mg, IR 10.5–22.1; p = 0.009; day 1: 5.25 mg, IR 2.1–13.3 vs. 13.3 mg, IR 6.7–23.8; p = 0.150). On the following days (day 2 and 3) there was no difference (MEQ day 2: 13.3 mg, IR 0.0–20.0 vs. 13.3 mg, IR 6.7–13.3; p = 0.708; day 3: 13.3 mg, IR 0.0–26.7 vs. 13.3 mg, IR 6.7–20; p = 0.825). In total MEQ was less for CILA without reaching statistical significance (Day 0–3 MEQ 39.6 mg (IR 10.9–70.5) vs. 59.6 mg (IR 42.4–72.9), p = 0.187).
Conclusion: CILA is an effective tool to reduce pain during the first 24 h after HARP. After that time its effect abates.

Clinical Kidney Allocation

BOS494 COLD ISCHAEMIA TIME (CIT) DOES NOT TELL THE WHOLE STORY: ANALYSIS AND OUTCOMES OF COMPONENTS OF CIT

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Background: Cold Ischemia Time (CIT) is an important variable in kidney transplantation. We divided the CIT into three components: Extraction Time (ET): time from initial cold perfusion to time of kidney in the box; Transport Time (TT): kidney in the box to kidney delivered; and Unit Time (UT): kidney delivered to the unit to kidney out of the box. We assessed their influence on functional outcomes and 1 year GFR.
Methods: Retrospective analysis on all deceased donor (DD) kidney transplants was performed in our unit from 09/2011- 03/2015. Univariate analysis of CIT and its components; multivariate analysis of impact of ET <60, 60–90 and >90 min and UT <4, 4–6 and >6 h on Immediate Function (IF), Delayed Graft Function (DGF), Primary Non Function (PNF) and 12 months GFR of kidney transplanted from Standard Criteria (SC) and Extended Criteria (EC) DBD and DCD donors was performed. Mann-Whitney, ANOVA, and Kruskal-Wallis tests were used as indicated.
Results: 218 transplants performed were analysed (47% EC) with a median CIT of 840 min. The median ET was 79 min and UT 592 min. ET alone did not have any impact on IF, DGF, PNF and GFR 12 months. When stratified to ET, CIT >14 h was predictably associated with significantly inferior GFR but not function. A UT >6 h did have an impact on overall number of DGF and PNF (p = 0.0127). Stratifying ET >60 min, revealed significantly more DGF and PNF in DCD vs. DBD (p = 0.0003) and ECD vs. SCD (p = 0.03). Similarly, a UT >6 h demonstrated a negative impact on EC vs. SC in both function (p = 0.0046) and 12 month GFR (p = 0.0031). Most importantly, EC kidneys fared significantly worse when subjected to an ET>60 min and UT>6 h, vs. SC kidneys (Function, p = 0.0004; 12 months GFR, p = 0.0183), a finding not seen with a shorter ET.
Discussion: CIT alone is an unreliable indicator of IF and 12 months GFR. UT is the major component of CIT, and along with ET, need to be taken into consideration when evaluating offers in particular from EC.

Clinical Kidney Donation and Donor Types

BOS495 DYNAMIC OF MEASURED GLOMERULAR FILTRATION RATE (MGFR) IN LIVING KIDNEY DONORS BEFORE AND AFTER KIDNEY DONATION

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Background: As kidney transplantation is regarded as the best therapeutic option for patients with end stage renal disease, a growing demand for donation organs is apparent. Hence living kidney donation is increasingly performed. This study aimed to evaluate the measured glomerular filtration rate in living kidney donors before and over the course of 3 years after living kidney donation. Additionally, the applicability of calculated GFR formulas after unilateral nephrectomy was evaluated.
Methods: Fifty living kidney donors were included in this prospective study. mGFR was measured before donation, three months and twelve months after donation by inulin-clearance (INUTest). Creatinine was evaluated as a routine parameter of kidney function on all evaluation appointments and later used for the calculation of GFR.
Results: Inulin measurements showed a mean mGFR of 96.73 ml/min/1.73 m^2 ± 16.5 before kidney donation. Three months after donation, mean mGFR was 73.57 ml/min/1.73 m^2 ± 13.74 and twelve months after donation 70.49 ml/min/1.73 m^2 ± 14.35. Linear regressions of mGFR and calculated GFR using creatinine-based formulas (MDRD and CKD-Epi) showed the following findings: MDRD before transplantation: R^2 = 0.2; MDRD three months after transplantation: R^2 = 0.2 and MDRD twelve months after transplantation: R^2 = 0.682. Linear regression of mGFR with CKD-EPI showed R^2 = 0.0043 before transplantation; R^2 = 0.187 three months after transplantation and R^2 = 0.807 twelve months after transplantation.
Conclusion: Measurement of mGFR by inulin-clearance proves a decrease in mGFR of less than 50% from preoperative values until 1 year after donation. This finding confirms a sufficient preservation of kidney function after living donation. Additionally, best correlation of mGFR with calculated formulas was found with the CKD-EPI formula. We therefore consider the calculation of GFR using CKD-EPI as most accurate after unilateral nephrectomy.

BOS496 MENTAL DISORDERS AMONG UNSPECIFIED LIVING KIDNEY DONORS

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Background: Psychosocial evaluation is performed in unspecified living kidney donation in an attempt to avoid mental disorders resulting from donation.
Methods: Potential unspecified donors who started the screening process between May 2000 and December 2016 were included. We studied all records of the routine medical checkups at 6 weeks, 1 year, 2 years and 3 years after donation.
Results: In total, 236 potential unspecified donors started the screening process. Eighteen (7.6%) were diagnosed with a mental disorder (mostly moderate to severe mood and psychotic disorders) and not accepted for donation, while 28 were not accepted because somatic contraindication, 33 withdrew consent for donation, 7 screenings were ongoing. of the 150 who donated, 11 (7%) reported psychopathology within 3 years after donation (posttraumatic stress disorder (n = 2), depression (n = 2), bipolar disorder with suicidal gestures (n = 2), unspecified psychiatric breakdown (n = 1), personality disorder not otherwise specified (n = 1) and depressive symptoms not meeting the full DSM-IV criteria (n = 3)). In total, of the 236 potential donors 29 (12%) of the potential unspecified living donors suffered from psychopathology. Four donors attributed their decrease in mental health to the donation process.

Conclusion: A small proportion (7%) of potential unspecified living donors were rejected due to psychiatric disorders. of the 150 persons that actually donated, 11 (7.3%) experienced mental problems during a 3-years follow-up. These figures are lower than the prevalence in the Dutch population (18%).

BOS497 EN-BLOC KIDNEY TRANSPLANTS FROM DONORS UNDER 2 YEARS OF AGE: A SINGLE CENTER EXPERIENCE

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Background: En-bloc transplantation of kidneys from brain-death small paediatric donors into adult recipients has been controversially discussed. They are still classified as marginal organs. Improvements in perioperative care have enhanced the acceptance rate for these organs. Herein, we present our recent experience with en-bloc kidney transplantation from paediatric donors ≤ 2 years of age into adult recipients.
Methods/Materials: Between January 2015 and December 2016 a total of five en-bloc kidney transplantations from paediatric donors ≤2 years of age into adult recipients were performed at our department. Mean donor age was 12.2 month (±8.6). The organs were retrieved en-bloc and transplanted into adult recipients. Mean recipient age was 39.8 years (± 11.4). Postoperative management consisted in 6 hourly sonographic controls, iv. heparinisation for the first 3 days and maintenance of the systolic blood pressure at ≤100 mmHg.
Results: In two out of five patients, the postoperative course was uneventful with immediately good graft function. In one case a delayed graft function occurred with the requirement of 4 dialyses, however, graft function continuously improved and the patient was released on the 13th pod with a serum creatinine of 2.7 mg%. In two cases an arterial graft thrombosis of the medially located kidney occurred on the 2nd pod, requiring unilateral nephrectomy of the affected graft. Both patients recovered well from this event and were dismissed in good conditions and dialysis-free on the 25th pod. of note, one case requiring unilateral nephrectomy was a recipient of en-bloc kidneys from a 3 days old donor with each kidney measuring 5.5 cm.
Conclusion: In times of organ shortage and increasing number of patients on the kidney-waiting-lists, there should be no age or kidney-size limitation in the acceptance of organs from very small paediatric donors.

BOS498 LIVING DONOR KIDNEY TRANSPLANTATION IN BLACK, ASIAN AND MINORITY ETHNIC PATIENTS; A SINGLE CENTRE CROSS SECTIONAL COHORT STUDY

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Introduction: Black, Asian and minority ethnic groups (BAME) constitute 11% of the UK population yet represent 30% of the national kidney transplant waiting list. Initiatives to address this disparity are underway including promotion of living donor kidney transplantation (LDKT) in BAME. Currently approximately one third of all kidney transplants in the UK are from living donors. The purpose of this study was to (i) assess BAME representation in our large ethnically diverse LDKT cohort (ii) identify strategies to promote LD in BAME.
Method: We undertook a retrospective cross sectional cohort study of all live related (LR) and unrelated (LU) adult KT at our unit between 1/1/10 and 1/8/15.
Results: 537 LDKT took place in the study period. 62% of recipients were male. Mean recipient age at transplant was 45.2 years. Mean living donor age was 45.0 years. *n* = 429 (79.9%) of the recipients were white. of the BAME recipient group, *n* = 53 (9.9%) were Black, *n* = 31 (5.8%) Asian, *n* = 4 (0.74%) mixed race, *n* = 7 (1.3%) Chinese/Oriental, *n* = 13 (2.4%) other

Table showing distribution of LU & LR KT in each ethnic group.

	Ethnic Group					
	White	Black	Asian	Mixed	Chinese	Other
LU KT	45% n=193	34% n=18	45% n=14	50% n=2	57% n=4	23% n=2
Pooled	n=18	n=2	n=1	-	-	n=1
Altruistic	n=26	n=4	n=2	-	-	-
Spouse	n=84	n=7	n=7	n=1	n=3	-
Partner	n=17	n=1	-	n=1	n=1	-
Other	n=48	n=4	n=4	-	-	n=1
LR KT	55% n=236	66% n=35	55% n=17	50% n=2	43% n=3	77% n=11
Sibling	n=104	n=17	n= 6	n=1	-	n=5
Parent	n=60	n=2	n=3	n=1	n=1	n=2
Son/daughter	n=49	n=8	n=6	-	n=2	n=3
Other	n=23	n=8	n=2	-	-	n=1

Conclusions: According to national figures our unit performs more BAME LDKT than average. Nevertheless our data highlights significant under representation of BAME on the LDKT programme. Except for Chinese recipients, LD were most likely to be a related sibling. In contrast to Caucasians, none in the 'other' group (majority being Middle Eastern) received a transplant from spouse/partner. Understanding the intercultural differences demonstrated in our LDKT cohort may help address BAME representation nationally and guide policy to promote LD in BAME.

Basic Kidney Donation and Donor Types

BOS499 "TALK ABOUT IT" EARLY EDUCATION OF PATIENT, FAMILY AND FRIENDS; A WAY TO PRE-EMPTIVE KIDNEY TRANSPLANTATION

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Background: Pre-emptive kidney transplantation offers the best treatment for patients with end-stage renal disease. Many patients find it difficult to talk with relatives and friends about their illness and treatment options and start with dialyses.
Methods: Every patient with end-stage renal disease is send by the nephrologist to the kidney failure team. First, the social worker visits patients at home for an intake. General information about future procedures is provided. Additionally they offer patients a home-based education of family and friends.

When the patient agrees, an informative gathering involving discussion about health status and treatment modalities is organised. This also includes data on patient survival on dialysis and after transplantation. Risks and benefits of living kidney donation (LKD) for recipient and donor are presented. Social workers closely cooperate with nephrologists and the nurse coordinator to make the topic of LKD more open to discussion at every patient contact.
Results: All patients appreciate the attention and support from the social worker, nurse coordinator and nephrologists on the field of LKD. Patients were relieved when the social worker initiated discussion about LKD. In the last 4 years (2013–2016) 58% of all patients who entered the program found one or more potential kidney donors and have the possibility of pre-emptive kidney transplantation. If all patients would have participated in home-based education overall percentages could have been higher. Home-based education results for 75% of participants in a potential kidney donor.
Conclusion: If renal replacement therapy is discussed, it is important that all involved disciplines inform and educate patient and family members about kidney disease and all treatment options, including pre-emptive kidney transplantation and living kidney donation. Family and friends can reflect on LKD. This increases the possibility of pre-emptive kidney transplantation.

Clinical Kidney Allocation

BOS500 A DISCRETE CHOICE EXPERIMENT (DCE) ON PATIENTS' TIME AND RISK PREFERENCES IN KIDNEY TRANSPLANTATION: PATIENTS' AGE AND WILLINGNESS TO WAIT (WTW) FOR BETTER ORGANS

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Background: WTW from the perspective of the patients themselves is unknown. We run a DCE to elicit patients' preferences, namely their risk attitude and time discounting.
Method: From April 2015–February 2017, 211 candidates (mean age 50 yrs) on the waiting list for kidney transplant were interviewed. 16 pairs of alternatives

were proposed: alternative differs along 4 attributes, waiting time, graft survival, infectious risk, neoplastic risk. Time attribute has 4 levels (6, 12, 36, 60 months), survival 3 levels (10, 15, 20 years) and both risks 2 levels (standard/increased). A mixture logit model was used to retrieve individual WTW and compare the entire distribution of preferences by different age groups.
Results : Older patients are willing to wait much less than younger candidates for extra year of graft survival. After age of 37, the effect of age on WTW for graft survival becomes negative. WTW for an extra year of graft survival is lower for females compared to males by about 1 month. The result is robust to a number of different model specifications. For standard infectious risk, females are willing to wait 8 months more compared to males. Having completed high school education compared to elementary education lowers WTW to avoid standard infectious risk by 7 months. No statistically significant difference in term of risk attitude among different age levels can be detected. Older patients have more heterogeneous preferences in terms of risk attitude than younger patients: for them the benefit of reducing waiting time and the potential cost of receiving an organ with augmented risk, are larger compared to the younger patients and this induces heterogeneity.
Conclusions: Our experiment suggests that pre-emptive transplantation with ECD to elderly patients maximizes the efficiency of allocation in terms of overall years of graft survival for transplanted organs and the patients' welfare.

Clinical Kidney Infection

BOS501 LIFELONG PROPHYLAXIS WITH TRIMETHOPRIM-SULFAMETHOXAZOLE FOR PREVENTION OF OUTBREAK OF *PNEUMOCYSTIS JIROVECII* PNEUMONIA IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Outbreaks of *Pneumocystis jirovecii* pneumonia (PCP) in kidney transplant recipients have been frequently reported worldwide, especially from Europa. Japanese kidney recipients as well as European have a greater chance of sharing time and space in outpatient clinics. Occurrence of a single case of PCP under such circumstances could easily result in a PCP outbreak. However, general guidelines propose only short-term individual prophylaxis with trimethoprim-sulfamethoxazole following kidney transplantation. We experienced three PCP outbreaks despite providing the recommended prophylaxis in this decade.
Methods: Occurrence of PCP in our hospital has reviewed since 2004. A total of 48 cases occurred from July 2004 through December 2014. Genotypes of *P. jirovecii* were determined in these cases.
Results: Three PCP outbreaks with three different genotypes of *P. jirovecii* in each outbreak were occurred with 2-year intervals in this decade. Molecular analysis showed that each intra-outbreak was caused by identical *P. jirovecii*, whereas inter-outbreaks were caused by different genotypes. Although term-limited prophylaxis was provided to all kidney recipients after each outbreak following identification of a single PCP case, additional outbreaks were not prevented because the universal prophylaxis had already completed when new case of PCP emerged. None of PCP case was observed over 2-year period after a lifelong prophylaxis strategy was adopted.
Conclusions: The contagious nature of *P. jirovecii* allows easy development of outbreaks of PCP in kidney transplant recipients under current immunosuppression. While the universal short-term prophylaxis is effective in controlling ongoing outbreak, lifelong prophylaxis should be considered to kidney transplant recipients to prevent new outbreaks caused by different genotypes intermittently.

BOS502 CARBAPENEM-RESISTANT *KLEBSIELLA PNEUMONIAE* (CR-KP) INFECTIONS IN KIDNEY TRANSPLANTATION

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Carbapenem-resistant *Klebsiella pneumoniae* (CR-KP) infections in solid organ transplant patients are progressively increasing, and are associated with worse outcomes, though various aspects, such as possible risk factors and therapeutic strategies, are still not well defined.

We conducted a retrospective matched-pair analysis in which we compared 28 recipients CR-KP-positive after kidney transplantation with 56 CR-KP-negative patients transplanted in the same period, during a CR-KP outbreak occurred in our hospital.

Two patients had only a CR-KP rectal colonization, while 26 patients developed a symptomatic CR-KP infection. Twenty-one of patients (80%) received a combined antibiotic treatment.

At the end of the follow-up, of the 26 infected patients, 11 (42.3%) experienced at least one episode of re-infection, 9 (34.6%) remained colonized, and 6 (23.0%) were CR-KP-negative. Two of the 11 patients with re-infection died, while nine were colonized at the end of the study.

The Kaplan–Meier curves evidenced a significant difference of graft and patient survival between the two groups (log-rank$<$0.05). The multivariate logistic regression analysis revealed that the Clavien-Dindo score was the only independent risk factor for CR-KP infection.

The study confirmed that a CR-KP positivity can strongly affect the outcome of a kidney transplant population. In severe CR-KP infections with sepsis, a combined antibiotic treatment seems to be achievable and effective.

BOS503 USING DONORS WITH FALSE POSITIVE HIV TESTS – AN UNEXPECTED BENEFIT OF THE HOPE ACT

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Background: Deceased donors are screened for HIV infection using anti-HIV antibody (Ab) and nucleic acid testing (NAT). Historically, organs were discarded in cases of a suspected false positive screen. Organs from donors with false positive HIV tests can now be used for transplants in HIV+ candidates under HIV Organ Policy Equity (HOPE) Act research protocols.
Methods: HIV false positive donors were deceased with a single positive HIV Ab or NAT test and no history of HIV infection (per medical record and Donor Risk Assessment Interview). HIV+ individuals enrolled in the HOPE in Action trial (NCT02602262) of HIV+ deceased donor transplants were eligible for transplant. HIV realtime qPCR testing (Abbott) was done to confirm all false positive donor cases.
Results: Between May and November 2016, 6 HIV false positive donors were identified. Median donor age was 24 years (range 7–44). Five were male. Three were labelled increased risk for infectious diseases transmission based

HIV-False Positive Donors

Characteristic	Donor 1	Donor 2	Donor 3	Donor 4	Donor 5	Donor 6
Age (yr)	25	44	32	23	19	7
Sex	Male	Male	Male	Male	Male	Female
Race	African American	Caucasian	Hispanic	African American	Caucasian	Caucasian
Blood type	O	A	O	A	O	O
KDPI	28	30	25	58	9	41
Cause of death	Head Trauma (Gunshot Wound)	CVA/Stroke	Head Trauma (Blunt Injury)	CVA/Stroke	Head Trauma (Gunshot Wound)	Anoxia (drowning)
Increased infectious risk	No	No	Yes	Yes	No	Yes
HIV antibody assay (result)	Bio-Rad GS HIV-1/HIV-2 Plus O EIA (positive)	Bio-Rad GS HIV-1/HIV-2 Plus O EIA (positive)	Abbott Prism HIV O Plus (positive)	Bio-Rad GS HIV-1/HIV-2 Plus O EIA (negative)	Bio-Rad GS HIV-1/HIV-2 Plus O EIA (negative)	Bio-Rad GS HIV-1/HIV-2 Plus O EIA (positive)
HIV nucleic acid test (result)	PROCLEIX ULTRIO Plus (negative)	Roche Cobas TaqScreen MPX Test, version 2.0 (negative)	Gen-Probe Procleix Ultrio TMA Assay (negative)	Gen-Probe Procleix Ultrio TMA Assay (positive) HBV, HCV, HIV, discriminatory (negative)	Roche Cobas TaqScreen MPX Test, version 2.0 (positive)	Gen-Probe Procleix Ultrio TMA Assay (negative)
Organs transplanted	Liver, 2 kidneys	Liver, 2 kidneys	Liver, 2 kidneys	Liver, 2 kidneys	Simultaneous liver-kidney, kidney	Double kidneys

on the Public Health Service (PHS Risk). Cause of death was trauma ($n = 3$), stroke ($n = 2$) and anoxia ($n = 1$). Four donors were HIV Ab positive/NAT negative and two donors were Ab negative/NAT positive; one positive NAT was a simultaneous screen for HIV/hepatitis B/hepatitis C but was negative for each by discriminatory NAT. HIV realtime PCR testing was negative in all 6. Fifteen HIV+ recipients received organ transplants from these donors (9 single-kidney, 1 double-kidney, 4 livers, 1 simultaneous liver-kidney).
Conclusion: The HOPE Act allows for the use of organs from deceased donors with suspected false positive HIV screening tests. This is an unexpected benefit that provides another novel organ source for HIV+ individuals and can help attenuate the national organ shortage.

BOS504 IMPACT OF URINARY TRACT INFECTION IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Background: Urinary Tract Infection (UTI) is the main cause of infectious complications in renal transplant (RT) recipients and could result in graft loss and mortality. However, the risk factors of UTI are controversial.
Materials and methods: This research was conducted in a Transplant Center in Tucuman from January 2011 to December 2015. The aim of this study was to evaluate the frequency, risk factors, causative pathogens and the impact on graft function and patient survival. This was a retrospective study. The population was divided in three groups: <30 days, 1 to 6 months and 7 to 12 months post-transplant.
Results: There were 126 kidney transplant recipients of whom 34 developed UTI during the first year (27%). The mean age was 48.2 ± 13.7 years and 19 of them were females (55.9%). Bacterial UTI was found in 89 specimen urine, 30 (33.7%) in the first 30 days, 38 (42.7%) from 1 to 6 months and 21 (23.6%) from 7 to 12 months. 16 patients (47%) had one episode and 18 two or more. The most prevalent pathogens were: Klebsiella pneumoniae (KPN) 44 (44.9%), Escherichia Coli (ECO) 27 (30.3%) and Enterobacter cloacae (ECL) 16 (18%). 51 (57.3%) had BLEE. Among the risk factors the only significant was the number of days hospitalized (21.5 vs. 14.5 days $p < 0.007$). 7 patients had the urinary tract instrumented. 4 of the 34 (11.8%) patients died because of UTI. We did not find any impact in graft function in the 3 periods studied.
Conclusions: Nearly one-third of RT patients had at least 1 episode of UTI in the first year post transplant. KPN was the most prevalent pathogen with high BLEE. We observed high mortality rate because of UTI.

BOS505 THE COST AND THE PRICE OF URINARY TRACT INFECTIONS FOLLOWING RENAL TRANSPLANTATION: A FOUR-YEAR SINGLE CENTER EXPERIENCE

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Background: Urinary tract infections (UTI) are the most frequent infectious complication following renal transplantation. Yet their impact on hospital admission rate, generation of antimicrobial resistance, and graft function is not well established.
Methods: This study is a retrospective review of renal transplant patients developing a urine-dip positive UTI severe enough to warrant hospital admission at our center between 01/01/2012 and 31/12/2015. Data collected included the hospital length of stay (LOS), re-admissions rates, urine culture results, presence of bacteraemia, and antibiotic treatment. The impact on graft function was determined in terms of acute kidney injury (AKI) – defined by a rise in creatinine >50% – at day 0 and day 90, graft loss and mortality at 1 year.
Results: We identified 88 patients accounting for 212 admissions with UTI. This represents 8.7% of all transplant patient admissions. Median LOS was 4 days, with a total LOS of 1278 days. Re-admission rate was 37.3% within 3 months, and 31.1% within 3 months to 1 year. The most common pathogens were *Escherichia coli* (46.7%), *Klebsiella* species (16.0%), *Pseudomonas aeruginosa* (6.1%), and *Enterococcus faecalis* (3.8%). Extended-Spectrum β-Lactamase (ESBLs) were isolated in 17.0% of samples. Bacteraemia occurred in 17.9% of cases. Nil significant growth was detected in 17.0% of urine cultures, of which 38.9% had documented antibiotic therapy prior to admission. Individual case studies demonstrate the generation of antibiotic resistance over subsequent admissions. AKI at day-0 was 50.9% and at day-90 was 7.5%. Graft loss and mortality at 1-year was 2.4% and 0.5% respectively.
Conclusion: UTIs post renal transplantation represent a significant cost to healthcare services in terms of length of hospital stay and readmission rates, as well as posing a substantial price to patients' disease burden with respect to the development of antibiotic resistance and adverse outcome on graft function.

Basic Kidney Infection

BOS506 CCR5-MEDIATED RECRUITMENT OF NK CELLS TO THE KIDNEY IS CRITICAL FOR RESISTANCE TO CANDIDA ALBICANS INFECTIONS

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We previously showed that CCR5 mediates recruitment of NK cells to the kidney after renal ischemia and reperfusion, which in turn induce the production of CCR5 chemokines by tubular epithelial cells. Recruited NK cells stimulate tubular epithelial cells to secrete CXCR2 chemokine through CD137 ligand, resulting in chemotaxis of neutrophils, major effectors for kidney ischemia-reperfusion injury. In this study, we investigated the involvement of CCR5 in host innate immune responses to *Candida albicans*, an opportunistic pathogen which infects the kidney of immunocompromised patients. CCR5-/- mice were shown to be highly susceptible to systemic *C. albicans* infections. A characteristic feature of infected CCR5-/- kidneys was decrease in levels of IL-23 and GM-CSF in the kidney. IL-23 was secreted from dendritic cells after *C. albicans* infection and GM-CSF was produced from NK cells in response to IL-23 in wild-type mice. Infusion of GM-CSF into CCR5-/- mice significantly recovered their ability to clear *C. albicans* from the kidney, while injection of IL-23 failed to induce production of GM-CSF. Taken together, our results indicated that CCR5-/- dendritic cells and NK cells have intrinsic defects in their ability to produce cytokines critical in resistance to anti-*C. albicans* infections.

Clinical Kidney Infection

BOS507 TRANSPLANTATION AND DIALYSIS CENTER BACTERIAL PROFILE ANALYSIS: NINETEEN-YEAR REPORT (1998–2016)

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We have examined the bacteriological tests results of 1282 patients in 1998–2016. In all patients bacteriological tests were performed because of suspected of infection.

The total incidence of bacterial pathogens in culture of blood, sputum, urine and wound discharge increased from 61% to 76%.

The part of Gram-positive bacteria monoculture has decreased (from 45% to 24%) and Gram-positive bacteria monoculture remained at the same level (37–40%). At the same time the frequency of the mixed flora is significantly increased (from 10% to 31%). In recent years half of the microbial associations consisted of in 40% Gram-positive and Gram-negative bacteria, in 19% of Gram-positive and fungi, in 19% of Gram-negative and fungi. In other cases observed ternary association. Thus, there has been a fundamental change in the nature of the microflora: the dominance of Gram-positive bacteria changed to Gram-negative, and the nature of the flora is usually mixed.

Gram-negative bacteria are the most common bacterial population in recent years. There are *Klebsiella pneumonia* (37%), *E. coli* (28%), *P. aeruginosa* (17%), *Acinetobacter* spp. (10%), *Enterobacter* spp. (8%). *Enterococcus* spp. (50%), *Staphylococcus* spp. (44%) and *Streptococcus* spp. (6%) are found among Gram-positive bacteria. Fungi of the genus Candida were marked in 16% of culture: *C. albicans* (40%) and *C. glabrata* (30%), *C. krusei* (8%). Differentiation to the species level is not performed in 22%.

The part of fungi in monoculture remained approximately at the same level (5–8%). The incidence of *C. glabrata* and *C. krusei* increased.

The most common Gram-positive bacteria have a high sensitivity to a number of antibiotics such as vancomycin and linezolid. We noted a growth of resistance of *Klebsiella* spp even to modern antibiotics. Increasing of antibiotic resistance of *E. coli* was mentioned.

Over the years, there was a great change in the nature and composition of the bacterial flora in patients of our center.

BOS508 ENDOTOXIN ADSORPTION IN PATIENTS WITH SEPSIS AFTER RENAL TRANSPLANTATION

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We studied the effect of endotoxin adsorption on renal graft function in gram-negative or mixed infections.
Methods: The procedures were performed using extracorporeal hemoperfusion cartridge Toraymyxin PMX-20R (Toray, Japan) or LPS Adsorber (Lund, Sweden). We compared the outcomes of the main group, numbering 28 patients with a comparison group, numbering 25 patients. In all patients of the

main group we applied the selective endotoxin adsorption. All patients were diagnosed with gram-negative or mixed sepsis with different etiology.
Results: Usually in both groups urine output was significantly reduced. There was observed an increase of daily diuresis, mainly, we believe, as a result of adequate fluid resuscitation. The differences between the groups was not significant. The dynamics of diuresis in patients of the main group was more physiological. Creatinine clearance graft function has more injured than excretion of fluid. In most patients a marked increase in serum creatinine. In patients of the main group showed a strong trend to normalization of azotemia after one or two days of treatment, when sessions of endotoxin adsorption were performed. Thus, the decrease of serum creatinine in the main group was more expressed and significantly different from the comparison group of patients who have not had the adsorption of endotoxin. Glomerular filtration rate were also significantly improved in main group patients. Resistivity index in patients of comparison group was assessed not as detailed as in the main group and it cannot compare the groups properly. But it was found that in the result of generalized infection, there was an increase in resistivity index. As a result of the therapy and endotoxin adsorption a significant decrease of this index was showed.

We observed a better survival in recipients of the main group. This was better showed in the later stages of treatment. However, in the case of multiple organ failure in both groups the mortality was 100%.

BOS509 HOST BUT NOT PATHOGEN FACTORS PREDISPOSE TO KLEBSIELLA PNEUMONIAE UPPER URINARY TRACT INFECTIONS IN RENAL TRANSPLANT PATIENTS

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Background: Klebsiella pneumoniae is a frequent cause of nosocomial infections in immunocompromised patients including upper urinary tract infections (UTIs), but the role of genetic virulence factors (VFs) and host factors in upper UTIs development and outcome is ill-defined.
Methods: Patients' clinical and demographic data were registered prospectively. Phylogenetic background of K. pneumoniae isolates was analyzed by PCR Melting Profiles (MP) and the following VFs genes: *fimH*-1, *uge*, *irp*-2, *kpn*, *ycf*M, *mrk*D, *rmp*A, *mag*A, *hly*A, *cnf*-1 by multiplex PCR. VFs incidence was compared between RTx and non-RTx patients.
Results: We studied urine cultures and clinical data from 41 consecutive episodes of Klebsiella pneumoniae UTI in 37 RTx recipients, including 44% of male gender, with mean age of 54 $\pm$ 14 years. There were 19 episodes of asymptomatic bacteriuria (46%), 9 lower UTIs (22%) and 13 upper UTIs (32%) including 3 cases of urosepsis. 83% of isolated strains were ESBL+, while there were no carbapenemase producing strains. PCR MP typing showed a diverse population with 36 different genetic profiles, among which 4 profiles appeared in isolates from two or more patients, suggesting nosocomial infections. VF gene profiles were highly homogenous. Vesico-ureteral reflux or strictures at the uretero-vesical junction and lower urinary tract malformation as underlying cause of CKD emerged as independent predictors of Klebsiella pneumoniae upper UTIs (OR 20.00 with CI 3.8 – 106.1, $p < 0.001$), while we did not find any association between virulence factors profile and developing upper UTIs. No significant difference in the frequency of all investigated virulence genes was found between RTx patients and control group ($n = 15$).
Conclusions: Klebsiella pneumoniae upper UTI may be a marker of urine flow impairment e.g. vesico-ureteral reflux or strictures at the uretero-vesical junction. Bacterial VFs could not discriminate between upper and lower UTIs.

Clinical Others Infection

BOS510 *LACTOBACILLUS PLANTARUM 299V* PREVENTS *CLOSTRIDIUM DIFFICILE* INFECTION IN PATIENTS TREATED IN THE TRANSPLANTATION AND NEPHROLOGY WARDS

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Background: *Lactobacillus plantarum 299v* (LP299v) has been introduced into the clinical practice in order to reduce gastrointestinal symptoms during antibiotic exposure. However it remains controversial whether or not probiotics are also effective in the prevention of *Clostridium difficile* infections (CDI) among patients receiving antibiotics.
Aim of the study: The aim of this clinical, retrospective, single-centre study was to analyze the *C. difficile* infections among patients receiving antibiotics and hospitalized in the period before and after initiation of LP299v routine use, as a prevention of CDI, in the nephrology and transplantation ward.
Methods: Among 3533 patients hospitalized in the ward during 2 years (October 2012–October 2013 and December 2013–December 2014) 23 patients with CDI were diagnosed. Since November 2013 prevention of *C. difficile* infection with the oral use of LP299v was performed in all patients treated with antibiotics and who were at a high risk of developing CDI (patients after organ transplantation and receiving immunosuppressive drugs for any other reasons). For the further analysis the observation period was divided into two twelve-months periods, namely: period 1 before (October 2012–October 2013) and period 2 after initiation of LP299v use as the prophylactic manoeuvre against CDI (December 2013–December 2014).
Results: A significant ($p = 0.0001$) reduction of the number of cases with *C. difficile* infection was found in period 2 (after beginning of LP299v routinely used, $n = 2$; 0.11% of all hospitalized patients) compared to the previous 12-months (period 1 of observation, $n = 21$; 1.21% of all hospitalized patients).
Conclusion: Routine use of *Lactobacillus plantarum 299v* during treatment with antibiotics may prevent *C. difficile* infection, particularly in patients at high risk of such infection hospitalized in the transplantation and nephrology wards.

BOS511 A PROSPECTIVE, PHASE 2, COMPARATIVE STUDY OF ORAL SCY-078 VS. STANDARD-OF-CARE FOLLOWING INTRAVENOUS ECHINOCANDIN THERAPY IN THE TREATMENT OF INVASIVE CANDIDIASIS (INCLUDING CANDIDEMIA)

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Background: Solid organ transplant patients are prone to fungal infections. SCY-078 is an oral and (intravenous) IV, semi-synthetic triterpenoid antifungal, in development for the treatment for fungal infections caused by Candida and Aspergillus species. The purpose of this study was to evaluate the safety of 2 dosing regimens of oral SCY-078 in subjects with invasive candidiasis (IC), to identify the dose to achieve a target exposure (15.4 μM/h) in >80% of the intended population, and to assess the efficacy of orally administered SCY-078 vs. standard of care (SOC) following initial IV echinocandin therapy.
Methods: All subject with documented IC received an IV echinocandin for 3 to 10 days and were subsequently randomized to receive step-down oral therapy in a 1:1:1 ratio to one of the 3 treatment arms: oral SCY-078 1000 mg loading dose followed by 500 mg QD, or oral SCY-078 1250 mg loading dose followed by 750 mg QD, or SOC (oral fluconazole 800 mg loading followed by 400 mg QD or IV micafungin 100 mg QD) for up to 28 days. Plasma samples from SCY-078 subjects were collected to evaluate exposure by population PK modeling. Safety was assessed throughout the study
Results: Out of 27 subjects enrolled, 7 were randomized to receive SCY-078 500 mg, 7 to receive SCY-078 750 mg, 8 to receive the SOC (7 received fluconazole and 1 received micafungin due to fluconazole-resistant isolate) and 5 did not meet criteria for randomization. The rate of adverse events (AEs) and serious AEs were similar among subjects receiving SCY-078 or fluconazole. The most common AEs for all groups were gastrointestinal (GI); diarrhea, abdominal pain, nausea and vomit GI events were mild or moderate; none resulted in discontinuation. Efficacy as measured by favorable global response rates were reported among all groups.
Conclusions: The oral dose of SCY-078 estimated the target exposure in subjects with IC is 750 mg QD. This dose was well-tolerated and achieved favorable global response rate similar to SOC.

Clinical Kidney Infection

BOS512 EPIDEMIOLOGY AND OUTCOME OF TUBERCULOSIS IN IMMUNOCOMPROMISED PATIENTS IN A TERTIARY CARE HOSPITAL

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Background: The United States Renal Data System (USRDS) showed 1.2 and 1.6% incidences of tuberculosis (TB) in patients on peritoneal and hemodialysis, respectively. Kidney transplant (KTX) patients have higher rates.

We studied the epidemiology and outcome of TB in patients with kidney dysfunction in a tertiary care hospital in last decade.
Methods: We examined data of patients with TB with and without kidney dysfunction from 2006 to 2015 through an electronic system. Statistical analysis was completed using Stata software, Chicago, IL, USA.

Results: We found 581 patients with active TB and 37 with renal dysfunction including chronic kidney disease (CKD), hemodialysis (HD) and KTX. No difference was found in the prevalence, age or gender predilection and the main predisposing factors were kidney transplantation, diabetes and glomerulonephritis.

The incidence of TB is 3% per 100 000. The number of patients per year with active TB ranges from 52 to 128 and 3 to 4 in the general population and kidney dysfunction group, respectively.

Sixty-five percent of patients with kidney dysfunction had pulmonary TB, 5% had pleurisy and 30% had extra-pulmonary TB. Eighty-four percent of patients with kidney dysfunction completed the course of treatment with 16% treatment failure and 0.4% developed multidrug-resistant TB; 8% were lost to follow-up and 8% died during the treatment period.

Conclusion: The incidence and prevalence of TB in people with kidney dysfunction is nearly the same [LC1] despite an increase in patient load. Improvement in registries and screening is required to enhance the capturing rate and detection among this group, as well as providing accurate data to health authorities and the public about the magnitude, future trends, treatments and outcomes regarding TB in kidney dysfunction.

BOS513 VALUE OF PERIOPERATIVE GENITOURINARY SCREENING CULTURE IN PREDICTING EARLY URINARY TRACT INFECTION AFTER RENAL TRANSPLANTATION

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Background: We aimed to assess whether patients colonized with certain organisms in the genitourinary tract will have greater urinary tract infection (UTI) risk during the post-transplantation period, and whether information on the perioperatively colonized organisms may help identify the causal organisms during early UTI.

Methods: We retrospectively reviewed the culture results of preoperative urinary, preoperative urethral swab, and postoperative urinary catheter tip specimens of 420 patients who had undergone renal transplantation between July 2005 and June 2010. The colonization status was compared to the culture results during the first UTI episode within 6 months after transplantation.

Results: Common uropathogens were observed in 8 (1.9%) preoperative urinary, 68 (17.8%) preoperative urethral swab, and 73 (19.0%) postoperative urinary catheter tip specimens. Thirty-seven (11.7%) patients developed early UTI, and the presence of uropathogens in the perioperative genitourinary specimen was positively associated with a higher early UTI risk (hazard ratio, 2.73; 95% confidence interval, 1.43–5.21, $p = 0.002$). However, the actual causal organism during UTI was observed perioperatively only in 15 patients (40.5%). Neither colonization by uropathogens nor early UTI was associated with the subsequent development of acute cellular rejection, although early UTI was associated with 5-year graft survival.

Conclusion: Renal transplantation patients who were colonized with common uropathogens were more likely to develop early UTI. However, the usefulness of the culture results of perioperative colonizers in predicting the causal organism during early UTI seems limited due to the low concordance rate.

Clinical Pancreas/Islet Infection

BOS514 FACTORS IN ASSOCIATION WITH SEPSIS DIFFER BETWEEN SIMULTANEOUS PANCREAS/KIDNEY AND SINGLE KIDNEY TRANSPLANT RECIPIENTS

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As immunosuppressive therapy and allograft survival have improved in simultaneous pancreas/kidney transplant recipients (SPKTRs), the increased incidence of infection has become a major hurdle of disease-free survival. An analysis of SPKTRs with respect to risk factors for sepsis, microbiological characteristics, and its impact on patient and allograft outcomes is lacking.

We studied all primary SPKTRs and primary deceased-donor kidney transplant recipients (KTRs; <65 years) at our transplant center between 2005 and 2015 for the development of sepsis. 36 of 134 SPKTRs (26.9%) and 61 of 538 KTRs (11.3%) were diagnosed with sepsis. A control of 98 SPKTRs without sepsis was used for comparison.

SPKTRs were more likely to develop sepsis compared to KTRs ($p < 0.001$). While urosepsis was less common among SPKTRs (45%) compared to KTRs (65%), pneumonia (33%) and peritonitis (15%) as site of infection were more frequent ($p < 0.05$). Here, gram-positive and fungal sepsis were more common among SPKTRs ($p < 0.05$). Onset of sepsis was earlier in SPKTRs with a median of 6 months posttransplantation compared to KTRs with a median of 19 months posttransplantation ($p < 0.05$). Mortality from severe sepsis/septic shock was 29% among SPKTRs compared to 58% among KTRs. Among SPKTRs, female sex, low body mass index, CMV seronegativity, CMV disease, and acute cellular rejection increased the risk of sepsis ($p < 0.05$). SPKTRs with sepsis showed comparable patient, kidney, and pancreas allograft survival compared with SPKTRs without sepsis ($p > 0.05$), but superior patient and kidney allograft survival compared to KTRs with sepsis ($p < 0.05$).

Differences of incidence, site of infection, causative pathogens, and onset of sepsis between SPKTRs and KTRs may be attributed to more intense immunosuppression, major surgery, and complications of diabetes among SPKTRs. Despite the higher incidence of sepsis among SPKTRs, however, mortality related to sepsis presents lower among SPKTRs compared to KTRs.

Clinical Kidney Surgical Technique

BOS515 SURGICAL PROPHYLAXIS OF LYMPHOCELE AFTER KIDNEY TRANSPLANTATION

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Background: Despite the accumulation of experience and improvement of equipment and operation facilities, a significant problem remains surgical postoperative complications. Lymphocele is the most frequent complication that can be observed in 34% of kidney allograft recipients.

Symptomatic lymphocele often causes pain. External compression of ureter renal allograft leads to hydronephrosis and loss of graft function. Compression of the bladder can cause incontinence. In this case disorder of venous outflow can lead to venous thrombosis of kidney graft and lower limbs.

Material and methods: We report the analysis of kidney transplantation results within 66 patients in order to investigate specific pathogenetic prophylaxis of symptomatic lymphocele after kidney transplantation.

There were 37 (56.1%) men, 29 women (43.9%). Patients age was 33.4 ± 12.4 years. Based on the aim of the study patients were divided into two groups – I group with standard prophylaxis – 31 (47%) and II group – specific prophylaxis of lymphocele by using a high-frequency electric welding ("PATONMED") and Valleylab™ LS10 Generator (LigaSure™ Technology), there were 35 (53%) patients. We analyzed ultrasonography results on 1, 2 and 6 weeks after operation.

Results: In I group we discovered 5 (16%) symptomatic lymphocele, at the mean period about 6 weeks after transplantation. For these patients we performed surgical treatment. Good result ($p = 0.013$) was revealed in II group who were undertaken intraoperative lymphostasis by using a high-frequency electric welding. There wasn't any lymphocele diagnosed in this group of patients.

Conclusions: According to our data the significant risk factor of symptomatic lymphocele was the quality of intraoperative lymphostasis. Using of the high-frequency electric welding during the operation prevents lymphocele after kidney transplantation.

BOS516 EVALUATION OF AXIAL AND CORONAL SIZES OF POSTOPERATIVE LYMPHOCELE USING MULTIDETECTOR COMPUTED TOMOGRAPHY IN KIDNEY TRANSPLANT RECIPIENTS: PREDICTION OF SYMPTOMATIC LYMPHOCELE

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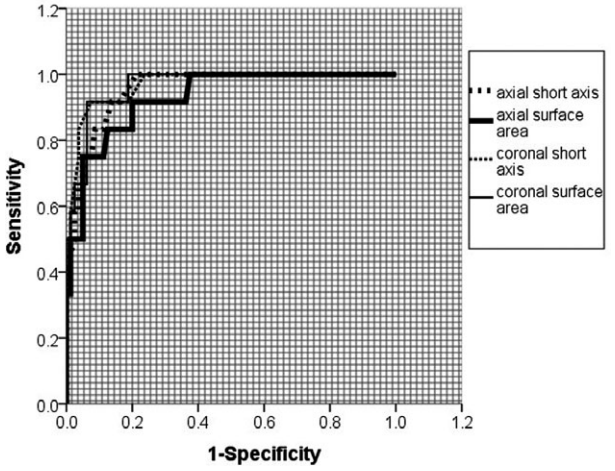
Background: To evaluate the sizes of postoperative lymphocele on the coronal and axial reconstruction planes, respectively using multidetector computed tomography (MDCT) in kidney transplantation recipients.

Materials & Methods: We evaluated 92 recipients who underwent MDCT of the abdominopelvis at 1 month after kidney transplantation. The axial short axis, axial surface area, coronal short axis and coronal surface area of lymphocele were measured by the reconstructed MDCT coronal and axial images. Depending on the clinical manifestations and radiologic findings of the recipients, all lymphocele were classified into symptomatic and asymptomatic. We compared the suitability of the size measurement on coronal and axial planes by MDCT reconstruction for symptomatic lymphocele in kidney transplant recipients with Spearman's correlation analysis and comparisons of receiver operating characteristic (ROC) curves.

Results: Areas under ROC curves were 0.957 and 0.928 for axial short axis and axial surface area and 0.968 and 0.966 for coronal short axis and coronal surface area. In pairwise comparison of ROC curve of the parameters for symptomatic lymphocele, the coronal measurement was more significant than the axial measurement (short axis, $p = 0.357$; surface area, $p = 0.047$)

Conclusion: For the prediction of symptomatic lymphocele by MDCT, the coronal measurement of postoperative lymphocele can bring a significant improvement in diagnostic performance over axial ones in kidney transplant recipients.



BOS517 OUTCOMES OF 335 PEDIATRIC KIDNEY TRANSPLANTS

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Introduction: Renal transplantation (RT) plays an important role in the treatment of end-stage kidney disease to prolong and improve the quality of life of pediatric patients. This study aims to evaluate the outcomes of pediatric RT in our center.
Materials and methods: Since November 1975, we performed 2646 RT procedures at two different centers by the same transplantation team. 335 were children (age $\leq$ 18 years) and we reviewed their medical records for the following: primary cause of liver failure, age and weight at time of transplant, type of graft, and medical outcomes of the recipient and donor. 110 (32.8%) were deceased donor transplants and 225 (67.2%) were living donor transplants. At our institution, we perform renal arterial anastomoses and ureteral anastomoses by means of a corner saving technique. There was no major donor morbidity and no donor mortality.
Results: 210 of the patients were female and 125 were male with a mean age of 13.6 $\pm$ 4.1 years (range, 1–18 years). During the early postoperative period we had 2 renal artery thrombosis (RAT), 1 renal artery kinking (RAK) 2 renal vein thrombosis (RVT), and 2 renal vein kinking (RVK). We performed surgery in 6 patients. We performed thrombectomy for RAT and RVT and we rearranged the position of grafts for renal artery or renal vein kinking. Urinary leak was revealed in 6 patients during the early postoperative period. During the late follow up period, renal arterial stenosis was identified in 3 patients and they were managed with percutaneous angiography and stenting. The 5-year patient survival rates were 91.9%. There were 27 patients who died during follow-up period. One patient died at the early stage of transplantation due to intracranial hemorrhage. 26 patients died at the late follow up period (15 urinary sepsis; 4 ARDS; 4 cardiac deaths; 2 cranial hemorrhages; 1 traffic accident).
Conclusions: Graft survival dramatically increased over the past years and is now superior to those observed in adult RT.

BOS518 RECONSTRUCTION OF THE PELVIS AND URETER OF THE RENAL GRAFT AFTER TOTAL NECROSIS OF THE URINARY EXCRETORY SYSTEM

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Urological complications are responsible for a large part of morbidity and mortality in the post-renal transplantation.
Objective: To report a case of complete pelvic and ureter necrosis, treated with pelvic and ureteral reconstruction, from the native ureter on the same side.
Case report: I. T. M, 36 years old, male, with chronic renal disease of unknown etiology, submitted to hemodialysis treatment 2 years ago, performed a kidney transplant with a living donor, identical HLA, Hospital Antônio Targino, Campina Grande, PB. The transplanted kidney was the left one, the clamping time was 1 h and 42 min, anastomosis of the renal vein with the common iliac vein and the renal artery with the external iliac artery, without intercurrences during the procedure. There was diuresis and decrease of urea and creatine by 50%, in the 1st day. On the second day, serum creatinine increased from 3.9 mg/dl to 7.93 mg/dl and urea from 72 mg/dl to 125 mg/dl. On the following day, USG was performed, from which hydronephrosis was detected in the graft. Necrosis of the ureteral implant was observed in the urinary bladder. After surgical reintervention, complete necrosis of the ureter and renal pelvis was identified. The pelvis and ureter were resected to the intra-renal portion and from the native ureter on the same side, deep pelvic anastomosis and double J stent implant and nephrostomy were performed.
Result: Restoration of renal function and urinary transit, in the first postoperative days, the stent were withdrawn with thirty days, without further complications.
Conclusion: Despite the severity, which represents complete necrosis of ureter and pelvis, reconstruction from the native ureter with deep intra-renal anastomosis was a successful procedure that restored urinary tract and renal function in this case.

BOS519 SETTING UP A DE NOVO ROBOTIC KIDNEY TRANSPLANT PROGRAMME – 10 STEPS IN SAFETY

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Background : Robotic-assisted kidney transplantation (RAKT) offers a minimally invasive surgical solution to patients with renal failure. The study aims to review the process of safely starting-up a robotic kidney transplant program *de novo*.
Methods : A multi-modality approach was taken to prospectively develop a safe method of introducing RAKT in a unit with minimal robotic expertise. This consisted of 4 processes: mentorship/proctorship, training/simulation, safety systems development and learning-curve negotiation.
Results : Initial expertise was acquired by travelling to the highest-volume RAKT centre in the world to observe a successful programme in-situ (Step 1). Collaboration with in-house urology specialists facilitated access to a robotic surgery system (Step 2). The in-built VR simulation module was used to practice basic robotic skills (Step 3), progressing to task-trainer exercises (Step 4) and tissue-based simulation using cadaveric vessels (Step 5). Mentorship was provided by robotic surgery experts overseeing the first three cases. In additional cases advice was available via online communication (Step 6). Expert group consensus was used to develop a RAKT-specific surgical safety checklist to prevent perioperative errors (Step 7). Structured multi-disciplinary team-debriefing at the end of each case was used to identify areas of improvement which were included in the subsequent cases' pre-operative brief and checklist (Step 8). Judicious early patient selection should avoid those with previous transplants, adhesions, hernias, obesity or polycystic kidneys (Step 9). Meticulous follow-up of outcomes and enrollment in a national registry are needed to facilitate good clinical governance (Step 10).
Conclusions : The 10 steps identified may advise other centres on how to mitigate the risks associated with starting a new RAKT programme. Further implementation analysis of the programme is needed to ascertain how well it's being embedded within the current service.

BOS520 EFFICACY OF USING FLOSEAL® TO PREVENT POST KIDNEY TRANSPLANTATION LYMPHOCELE FORMATION

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Background: Lymphocele associated with renal transplantation is still the most common surgical complication nowadays. We investigate the efficacy of using FloSeal® to reduce the incidence of post renal transplantation lymphocele.
Methods: We retrospectively reviewed the data of renal transplantation performed in two transplant hospitals in Hong Kong. We retrieved data from January 2004 to June 2016 and FloSeal® was applied during kidney transplantation since May 2013. In both hospital, FloSeal® was applied over the hilar region of graft kidney, segment of iliac artery dissection and vascular anastomosis during renal transplantation. Patients' demographics and peri-operative parameters were analysed. For statistical analysis, Fisher's exact test was used for categorical variables and independent sample *t*-test and Mann-Whitney U test were used for continuous variables.
Results: Total 365 patients (312 (85.5%) cadaveric and 53 (14.5%) living-related renal transplantation) were included in this review. The mean age was 39.53 years old (range from 4 to 69 years old) and FloSeal® was applied in 117 (32.1%) patients. There was no significant difference in patients' demographics such as age, gender and duration of renal replacement therapy between the FloSeal® and non-FloSeal® groups. The incidence of symptomatic lymphocele formation was significantly reduced in FloSeal® group (5.2% vs. 16.1%, $p = 0.004$). Also, lymphocele formation was lower in FloSeal® group (13.9% vs.

25.4%, p = 0.014) as well. Surgical drain could be earlier removed (4.46 days vs. 6.21 days, p = 0.000). Total drain output was less in FloSeal® group (467 ml vs. 890 ml, p = 0.051) even though it was not statistically significant. No adverse effect associated with the usage of FloSeal® occurred.
Conclusions: The results of this study suggest that FloSeal® can reduce lymphocele formation after renal transplantation and associated intervention. It also helps decrease drain output and facilitate earlier drain removal.

BOS521 OPTIMIZING THE EFFECT OF PROPHYLACTIC PERITONEAL FENESTRATION IN PREVENTION OF POST KIDNEY TRANSPLANTATION LYMPHOCELE THROUGH CLIPPING

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Background: Lymphocele is one of the most frequent complications following Kidney transplantation (KTx). Peritoneal fenestration is one of the known preventive methods in this regard. We aimed to optimize the preventive effect of this method through clipping the margin of the peritoneal fenestration and compare the results without clipping.
Methods: We prospectively followed up 16 patients who underwent KTx with preventive peritoneal fenestration at the end of KTx, from which in 8 patients an additive clipping of the peritoneal fenestration margin was performed. An easy-flow drain was inserted for all patients through the skin in to the peritoneal fenestration.
Results: The demographic data, perioperative management and immunosuppressive therapy of the patients in two groups did not show any significant differences. Median follow-up was 167 (27–309) and 169 (15–602) days without and with clipping, respectively (p = 0.443). Days to remove the drain was 13 (3–30) without and 10 (3–20) with clipping (p = 0.349). The drainage volume at time of removal was 80 ml (30–210) without and 100 ml (25–310) with clipping (p = 0.401). Three of eight patients developed post KTX lymphocele in the group without, meanwhile no patient had post KTx lymphocele in the group with clipping (p = 0.200). One of these three patients underwent therapeutic laparoscopic fenestration and two others were treated with percutaneous drainage without recurrence during the follow-up period. No intraoperative or fenestration related complication occurred. Graft and patient survival were 100% in both groups.
Conclusion: Clipping the margin of the preventive peritoneal fenestration at the end of KTx is feasible and safe. In a small prospective collective, there was not significantly less post KTx lymphocele with clipping in comparison to without. Further prospective studies with high case volume are needed to prove the effect of clipping.

Clinical Others Surgical Technique

BOS522 MULTI-ORGAN RETRIEVAL FOLLOWING EXTENSIVE TYPE B AORTIC DISSECTION

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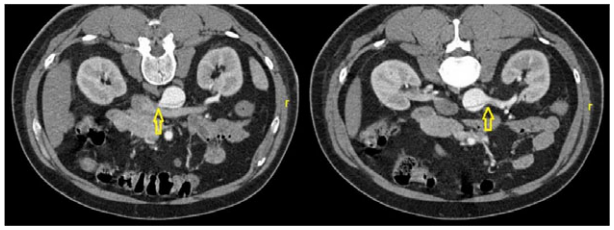
Freeman Hospital, United Kingdom

Introduction: Variations and abnormalities in organ vasculature are commonly encountered during organ recovery. Aortic aneurysms, abdominal and thoracoabdominal, offer peculiar and specific challenges to the organ retrieval team. Pre-operative planning and knowledge of abnormal anatomy will enable surgeons to salvage more organs for transplantation.
Case presentation: 65 year old male with a background of hypertension and hypercholesterolemia presented with extensive type B dissection. The false/true lumen extended from the left subclavian, through the thoracoabdominal aorta to the common iliac vessels as seen on computed tomography scan. Unfortunately he suffered a fatal ischaemic stroke during elective operative repair and was declared brain stem dead. His family were approached and consented for organ donation
Management: Organ retrieval was performed using two cannula approach. The cannulae were placed via right and left iliac vessels to both true and false lumens of the abdominal aorta respectively. The right renal artery (RA) had both a true and false lumen, with both lumens perfusing the kidney, while the left RA also having a true and false lumen was perfused via the false lumen, the true lumen ending as a blind pouch.

The liver arterial supply was via a left hepatic artery from coeliac trunk, and a right fully replaced artery from superior mesenteric artery (SMA). Both coeliac trunk and SMA originated from the true lumen of abdominal aorta.

The liver was recovered with an aortic patch and transplanted in our institution; both kidneys were recovered successfully and transplanted in other centres. All organs had a primary graft function.



Discussion: CT scans are not always available for review by retrieving surgeons before surgery. In this case the scans were essential to plan and optimise the organ recovery. Organs can be successfully retrieved from patients with complex thoracoabdominal dissections using multiple cannulae and a retrograde approach.

Clinical Liver Surgical Technique

BOS524 SYSTEMATIC REVIEW AND SURVEY ON A VERY RARE PROCEDURE IN LIVER TRANSPLANTATION – EMERGENCY TOTAL HEPATECTOMY FOLLOWED BY ANHEPATIC STATE

Patricia Sanchez, Michael Linecker, Mickael Lesurtel, Michelle De Oliveira, Christian Oberkofler, Pierre-Alain Clavien, Philipp Dutkowski, Henrik Petrowsky, Philipp Kron[1,2]
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Introduction: Emergency total hepatectomy followed by anhepatic state awaiting urgent liver transplantation has been reported for fulminant liver failure, hepatic trauma, and primary graft failure. In these life-threatening situations the first operation is to interrupt the devastating clinical condition originating from the toxic liver, followed by urgent liver transplantation (LT) in a second step. However, the reported experience of this procedure is rare. We performed a systematic review and international survey to evaluate current evidence and practice on this topic.
Methods: A systematic review of the literature on the topic "emergency total hepatectomy followed by anhepatic state awaiting urgent LT" was performed using MEDLINE, Cochrane Library, and Embase (PROSPERO 2016: CRD42016042922). In addition, an international survey among experienced transplant and hepato-pancreatico-biliary surgeons was conducted.
Results: 28 studies were identified. In 48% the procedure was used for PNF after LT, for fulminant hepatic failure in 28%, massive liver trauma in 22% and in 2% for other reasons. Median anhepatic time was 15 h (range 5–72.5). These findings were concomitant with the results of the survey. Out of 36 transplant centers contacted, a total of 33 centers (92%) replied. Twenty-eight out of 33 centers (85%) have indicated experience with this procedure (median 2 cases/center, range 1–12). More than half of the centers (52%) used this procedure for PNF after LT, 30% for fulminant hepatic failure, 12% as rescue procedure for massive liver trauma, and in 6% for other reasons. The median maximal tolerable anhepatic time was estimated at 37 h (range 3–120).
Conclusion: Both review and survey demonstrate that emergency total hepatectomy followed by anhepatic state awaiting urgent LT is a rare but life-saving procedure. Extended anhepatic periods of maximal 24 to 48 h appear to be tolerable when waiting for an organ. This procedure should belong into the tool box of every transplant surgeon.

BOS525 LOW PLATELET COUNTS AND PROLONGED PROTHROMBIN TIME EARLY AFTER OPERATION PREDICT THE 90 DAYS MORBIDITY AND MORTALITY IN LIVING-DONOR LIVER TRANSPLANTATION

Nobuhisa Akamatsu[1], Junichi Togashi[2], Junichi Kaneko[2], Junichi Arita[2], Yoshihiro Sakamoto[2], Kiyoshi Hasegawa[2], Norihiro Kokudo[2]
[1]Graduate School of Medicine, The University of Tokyo, Japan; [2]Artificial Organ and Transplantation Surgery Division, Department of Surgery, University of Tokyo, Japan

Objective: To investigate the association between platelet count/prothrombin time early after transplant and short-term outcomes among living – donor liver transplant (LDLT) recipients.
Summary background data: Postoperative platelet count and prothrombin time-international normalized ratio (PT-INR) were critical biomarkers in LDLT.
Methods: The study subjects were 445 initial LDLT recipients, and perioperative variables, including platelet count and PT-INR, were assessed for their

Figure 1

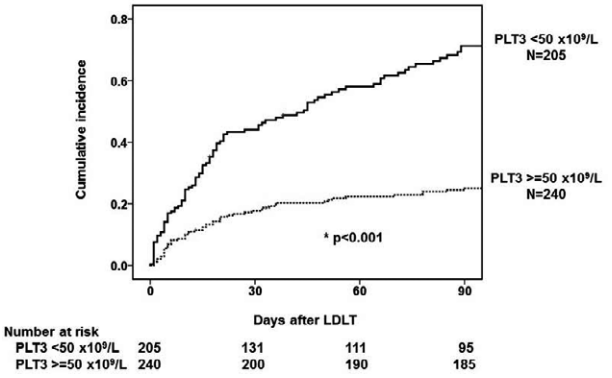
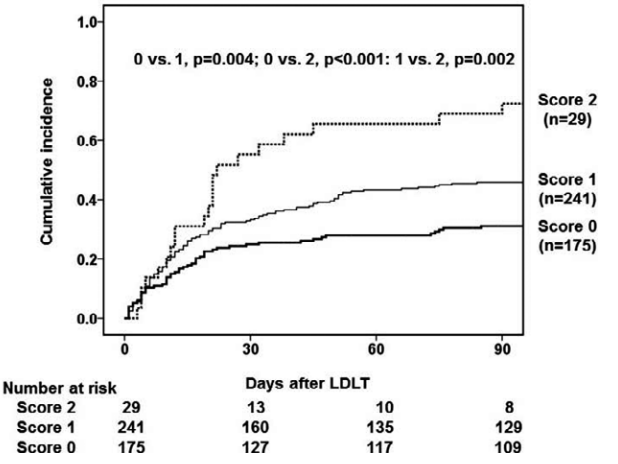


Figure 2



association with severe complications (Clavien-Dindo classification grade IIIb/IV) and mortality within 90 days after operation.
Results: Severe complications and operative mortality occurred in 161 patients (36%) and in 23 patients (5%), respectively. Cox regression analysis revealed that a high body mass index [hazard ratio = 1.2 (95% confidence interval = 1.1–1.4), p = 0.004] and low platelet count on POD3 [hazard ratio = 0.88 (95% confidence interval = 0.57–0.97), p < 0.001, Fig. 1] were independent predictors for grade IIIb/IV complications after LDLT, while high PT-INR on POD5 [hazard ratio = 1.1 (95% confidence interval = 1.1–1.3), p = 0.021] was the only independent factor for operative mortality. In addition, the prognostic scoring with low platelet count (<50 × 109/l) and prolonged prothrombin time (PT-INR > 1.6) within POD5, one point for each, was demonstrated to be useful in predicting the development of Clavien-Dindo grade IIIb/IV/V complications after LDLT (30% for Score 0, 46% for Score 1, and 72% for Score 2: 0 vs. 1, p = 0.004; 0 vs. 2, p < 0.001: 1 vs. 2, p = 0.002, Fig. 2).
Conclusions: PT-INR >1.6 and platelet count <50 × 109/l within POD5 were useful predictors of mortality and severe complications after LDLT.

BOS526 FENESTRATED STENT/GRAFT REPAIR FOR COMPLEX PSEUDOANEURYSMS AFTER LIVER AND PANCREAS TRANSPLANTATION

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Freeman Hospital / Institute of Transplantation / NIHR Blood Transplant Research Unit, United Kingdom

Background: Pseudoaneurysms after pancreas and liver transplantation are unusual but presentation can sometimes be catastrophic if they are not recognised early. Incidence rates are higher after pancreas transplantation (8%) compared to liver transplantation (1%). We describe the successful management of complex pseudoaneurysms following liver and pancreas transplantation using customised fenestrated stent grafts.
Methods: We present two cases, both male (ages 37/47 years). The first patient received a SPK prior to dialysis for diabetic nephropathy. His recovery was uneventful with insulin independence but early surveillance CT suggested small volume vessel arterial thrombus managed with therapeutic LMWH. An incidental 13 mm pseudoaneurysm involving the right common iliac artery and Y graft was demonstrated at 3 months postoperatively. The second patient underwent OLT for autoimmune hepatitis complicated by a late arterial thrombus of his infra-renal aortic/iliac conduit. Fungal organism was cultured from the liver explant following retransplantation. At 4 months follow up he was noted to have mildly deranged LFTS and a CT confirmed a 5 cm pseudoaneurysm arising from his aortic conduit.
Results: Both patients were managed using customised fenestrated stent/grafts. Back bench fenestrations (6 and 7 mm) were tailor made for each patient under sterile conditions using a low temperature cautery pen and reinforced with a microsnare and PTFE sutures. Each graft was then repacked into the delivery system. The pseudoaneurysms were excluded with demonstration of adequate graft arterial flow on completion angiography. There were no complications or endoleaks and both patients remain well with good graft function.
Conclusion: Experience with endovascular stenting particularly with the use of this technique is limited. However, it is an acceptable and safe management option for patients with complex pseudoaneurysms following liver and pancreas transplantation.

BOS527 CLINICAL EXPERIENCE AND FEASIBILITY OF TOTALLY LAPAROSCOPIC LIVING DONOR HEPATECTOMY

Jae Min Chun, Yoon Jin Hwang, Young Seok Han, Heontak Ha
Kyungpook National University Hospital, Korea

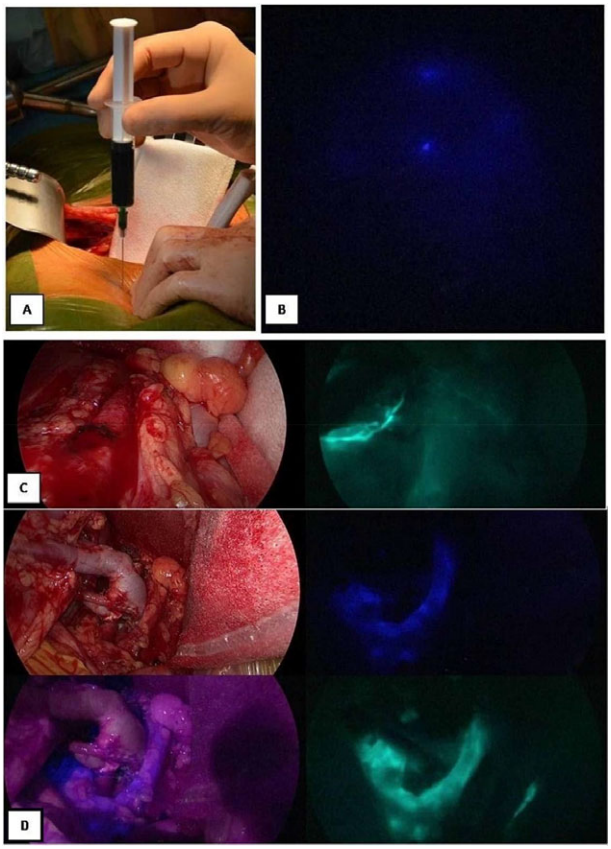
Background: Initial concerns regarding healthy donor's safety and graft integrity, need for acquiring surgical expertise in both laparoscopic liver surgery and living donor transplantation (LDLT) have delayed the development of laparoscopic donor hepatectomy in adult-to-adult LDLT. However, decreased blood loss, less postoperative pain, shorter length of stay in hospital, and excellent cosmetic outcome have well been validated as the advantage of laparoscopic hepatectomy. Hence, the safety and feasibility for laparoscopic donor should be further investigated. We report initial experiences and adequate inclusion criteria for totally laparoscopic living donor right hepatectomy (TLLDRH).
Methods: TLLDRH in 8 cases were performed from May 2016 up to Nov 2016. For this procedure, the donors' right portal vein with long segment of more than 5 mm were preferentially included. The bile duct anomaly was preoperatively evaluated with magnetic resonance cholangiopancreatography. The 1st case used 2D conventional rigid 30° rigid laparoscopic system and the next 7 cases used 3D flexible laparoscopic system.
Results: In 6 cases, hepatic duct anomalies were identified. Mean operation time was about 463 min and the warm ischemic time was within 15 min. During operation, there was no transfusion and the inflow control like Pringle maneuver was not used at all. V5 or V8 were reconstructed in 7 cases and large right inferior hepatic vein was prepared for anastomosis in 3 cases. All grafts were removed through the supra-pubic transverse incision. The donors were discharged at 7 days after hepatectomy. We have not observed any complications in the early postoperative follow-up.
Conclusion: Conclusively, TLLDRH in adult-to-adult LDLT can be initially attempted after enough experiences of laparoscopic hepatectomy and LDLT. However, the true benefits of totally laparoscopic living donor right hepatectomy should be fully assessed through various experiences from multi-institute.

Clinical Kidney Surgical Technique

BOS528 REAL-TIME INTRAOPERATIVE FLUORESCENT LYMPHOGRAPHY A NEW TECHNIQUE FOR LYMPHATIC SPARING SURGERY

Giuseppe Ietto, Gabriele Soldini, Domenico Iovino, Marco Calussi, Cristiano Parise, Elia Zani, Veronica Raveglia, Matteo Tozzi, Giulio Carcano
Insubria University, Italy

Background: Many surgical procedures can produce persistent lymphorrhea, lymphoceles and lymphedema after lymph nodes and lymph vessels damages. Appropriate visualization of the lymphatic system is challenging. Indocyanine green (ICG) is a well-known non-toxic dye for lymphatic flow evaluation. ICG fluorescent guided lymphography has emerged as a promising technique for intraoperative lymphatic mapping.
Objective: We aimed to develop a high spatial resolution real-time intraoperative imaging technique to avoid or early recognize deep lymphatic vessels damage.
Methods: We intraoperatively performed ICG fluorescence-guided lymphography during a kidney transplant. ICG was injected in the subcutaneous tissue



of the patient's groin in the Scarpa's triangle (A). A dedicated laparoscopic high definition camera system was used.
Results: Soon after ICG injection, lymphatic vessels were identified in the abdominal retroperitoneal compartment as fluorescent linear structures running side by side to the iliac vessels (B-C). Surgical dissection was therefore conducted avoiding iatrogenic damages to major lymphatic structures. Another ICG injection at the end of the procedure confirmed that the lymphatic vessels were intact without lymph spread.
Conclusions: Intraoperative lymphatic mapping with ICG fluorescence-sensitive camera system it's a safe and feasible procedure. ICG real-time fluorescent lymphography can be used to avoid or early recognize deep lymphatic vessels damage and reduce post-operative complications related to lymphatic system.

Clinical Kidney Histology

BOS529 HISTOLOGIC VARIABLES OBTAINED BY 1-YEAR PROTOCOL BIOPSIES RELATE TO KIDNEY TRANSPLANT FAILURE SCORE

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Hospital Universitario Marqués De Valdecilla, Spain

Background: Progressive reduction in acute rejection rates has led to an improvement of kidney graft survival throughout the first year, but long-term graft attrition rates remain stable beyond this point. Predicting the outcomes of kidney transplant recipients at 1-year would be useful in order to identify those for whom interventions may be needed. On one hand, it is known that allograft histology obtained by 1-year protocol biopsies is independently related to death-censored graft survival. On the other hand, several clinical risk scores, such as Kidney Transplant Failure Score (KTFS), have shown a good ability to predict long-term graft outcome. The aim of our study was to analyze the relationship between 1-year histologic findings of protocol biopsies and KTFS.
Methods/Materials: Between 2012 and 2016, 85 protocol biopsies were performed at 1-year post-transplant in our center and each biopsy was scored according to Banff criteria. KTFS was calculated taking into account 8 pre- and post-transplant clinical and analytical variables.
Results: Mean KTFS was 6.3 ± 1.7. KTFS related to t ($r = 0.256$, $p = 0.018$), i ($r = 0.299$, $p = 0.005$), ci ($r = 0.326$, $p = 0.002$), ct ($r = 0.341$, $p = 0.001$) and ah ($r = 0.265$, $p = 0.014$), but not with g, v, cg, cv, ptc or mm. Mean KTFS values were higher in patients with higher scores of t ($p = 0.046$), i ($p = 0.008$), ct ($p = 0.007$) and ci ($p = 0.009$). After multivariate linear regression analysis, both i (β 0.507, 95% CI 0.011–1.004, $p = 0.045$) and ci (β 0.460, 95% CI 0.034–0.886, $p = 0.035$) related to higher KTFS, but only 14.7% of total variation in KTFS was explained by histologic scores.
Conclusion: A clinical scoring system predictive of long-term kidney graft survival such as KTFS relates to both acute and chronic histologic findings in 1-year protocol biopsies, although the degree of correlation was weak. Both clinical scores and histologic variables provide additional information to predict renal graft outcome.

Clinical Kidney Immunology

BOS530 DOES INDUCTION THERAPY WITH ATG PROTECT AGAINST ANTI-HLA ANTIBODIES PRODUCTION AFTER TRANSPLANTECTOMY?

Edoardo Melilli[1], Marta Lepore[1], Anna Manonelles[1], Jaume Martorell[2], Josepmaria Cruzado[1], Nuria Montero[1], Maria Meneghini[1], Luis Riera[3], Oriol Bestard[1]
[1]Renal Transplant Unit Hospital De Bellvitge, Spain; [2]Immunology Hla Laboratory – Hospital Clinic, Spain; [3]Urology Department – Hospital De Bellvitge, Spain

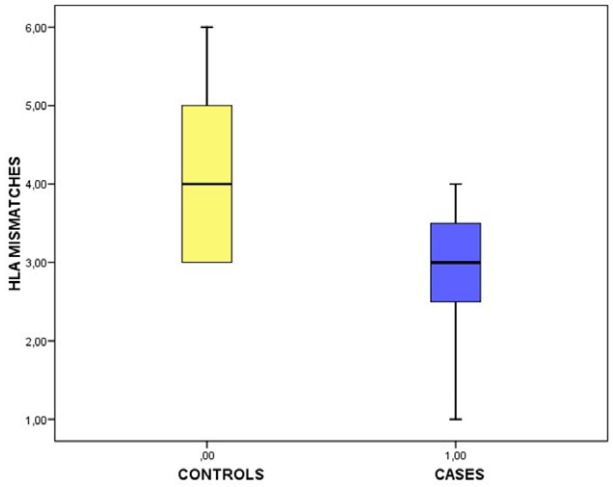
Background: Nearly one third of patients on waiting list for kidney transplant have preformed anti HLA antibodies. Transplantectomy (TRX) has been described as frequently, but no universally, associated to production of Donor Specific Antibodies. Factors related to lack of hyper-sensitization after a TRX are poor understood, so we decided to conduct a retrospective study, particularly to evaluate a possible protective role of induction therapy with ATG.
Methods/Materials: 46 patients transplanted at our hospital underwent early TRX due to non-immunological reasons in the last decade. Patients with pre transplant HLA antibodies were excluded (=6), as were patients without a complete immunological study conducted with Luminex technology before transplant and after TRX (=13). Immunosuppression was stopped after removal of the graft.
Results: Final population included 27 recipients who underwent TRX after a median time of 1 day (0–62). 20 of 27 patients (74%) had a positive Luminex assay at a mean time of 344 ± 267 days after transplantectomy, and were defined "controls". The other 7 patients (26%) remained negative at a mean follow up of 622 ± 583 days, and were defined "cases". All the cases had been treated with basiliximab, while 5/20 controls received ATG (25%), however this did not reach statistical significance (Table 1).

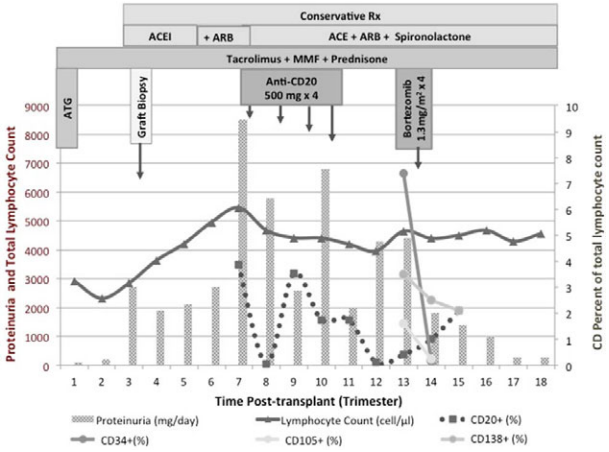
Final population included 27 recipients who underwent TRX after a median time of 1 day (0–62). 20 of 27 patients (74%) had a positive Luminex assay at a mean time of 344 ± 267 days after transplantectomy, and were defined "controls". The other 7 patients (26%) remained negative at a mean follow up of 622 ± 583 days, and were defined "cases". All the cases had been treated with basiliximab, while 5/20 controls received ATG (25%), however this did not reach statistical significance (Table 1).

	Cases (7)	Controls (20)	p
Age at transplant	62.7 ± 9.5	56.6 ± 13.4	0.21
Time on dialysis (months)	25 ± 15	21 ± 23	0.6
Sex receptor (M/F)	6/1	13/7	0.63
Donor type (DBD/DCD/LIVING)	6/1/0	14/3/3	0.38
Induction (BAS/ATG)	7/0	15/5	0.28
Blood transfusion peri. op (Y/N)	4/3	14/6	0.65
Re-transplant at follow-up (Y/N)	5/2	9/11	0.38

The only factors associated to the development of alloreactive antibodies were total MM and HLA-A incompatibility $p = 0.02$ (Fig. 1)

Conclusions: Induction therapy and the development of antibodies after transplantectomy were not related. Possibly, given the short time to transplantectomy observed, the small dose of ATG administered did not exert any kind of protective effect. As expected, patients with a better HLA compatibility have a reduced risk of sensitization. This result suggests that matching for HLA protect patients from developing de novo HLA antibody in case of an unsuccessful transplant.





Clinical Kidney Rejection

BOS531 IS TREATMENT OF CHRONIC ANTIBODY-MEDIATED REJECTION BY BORTEZOMIB EFFECTIVE?

Janka Slatinska, Eva Honsova, Tomas Rohal, Petra Bohacova, Petra Hruba, Ondrej Viklicky

Institute For Clinical and Experimental Medicine, Czech Republic

Background: Chronic antibody-mediated rejection (cAMR) remains a cause of graft loss in majority of kidney transplant recipients. The aim of this work was to analyze the efficacy and safety of administration of bortezomib (B) and rituximab-based treatment of cAMR.
Methods: We treated 9 patients with combined anti-humoral therapy. Our protocol consists of administration of B [1 cycle of 4 doses of bortezomib (1.3 mg/m^2)], small doses of intravenous corticosteroids, plasmaphereses and a dose of rituximab (375 mg/m^2). The protocol was applied to patients with stable renal function, but increasing donor-specific antibodies (DSA) and/or elevated proteinuria. Patients were followed for 18–36 months.
Results: Therapy of cAMR was administered to 9 patients after kidney transplantation with median peak PRA 46%, actual PRA 6%, mean HLA mismatch in HLA-A 1.2 $\pm$ 0.4, HLA-B 1.7 $\pm$ 0.5, HLA-DR 1.3 $\pm$ 0, with median of 5.8 years on dialysis. 2 patients underwent 1st kidney transplantation, while 7 patients retransplantation. Diagnosis of cAMR was made 1 year after transplantation (7–90 months). Based on therapeutic effect, 6 patients received 1 cycle, 1 patient 1.5 cycle and 2 patients were treated with 3 cycles of B. Using the bortezomib regimen in treating cAMR did not lead to decrease in DSA quantity. On the contrary, we observed increasing DSA in all classes (I, II a DQ with statistical significance, $p < 0.05$). No significant improvement of renal function was observed during the follow-up. 3-year graft survival after administration of the protocol with B is 80%. The side-effects observed were thrombocytopenia (22%), leucopenia (11%), colitis (11%) and pneumonia (11%).
Conclusions: Bortezomib was not effective against HLA class I and II antibodies. Patients with high amount of DQ DSA had worse fate than the others. Bortezomib-related toxicities were all transient and responded to conservative management. Therapy based on the protocol with B is not effective in the treatment of cAMR.

Clinical Kidney Immunology

BOS532 BORTEZOMIB AS A NOVEL THERAPEUTIC APPROACH TO EARLY RECURRENT POST-KIDNEY TRANSPLANT MEMBRANOUS GLOMERULONEPHRITIS REFRACTORY TO COMBINED CONVENTIONAL-RITUXIMAB THERAPY

Antoine Barbari[1], Rima Chehade[1], Hala Kfoury Assouf[2], Gaby Kamel[1], Mahassen Jaafar[1], Ayman Abdallah[1], Sylvana Rizk[3], Marwan Masri[3]

[1]Rafik Hariri University Hospital Lebanon; [2]King Saud University, Saudi Arabia Saudi Arabia; [3]Transmedical For Life, Lebanon

We report a case of early recurrent post-transplant membranous glomerulonephritis (RPTMGN) following cadaveric kidney transplantation. Patient received induction therapy and was discharged with a serum creatinine of 0.78 mg/dl on triple maintenance immunosuppressive therapy including Tacrolimus, Mycophenolate Mofetil and Prednisone. At seven months post-transplant, graft biopsy for new onset isolated proteinuria (2.7 g/day) revealed stage II recurrent membranous glomerulonephritis. In the face of partial remission with persistent proteinuria despite stable ideal body weight, well-controlled arterial systolic blood pressure between 110 and 120 mmHg and total CD20+ cells eradication following combined conservative-Rituximab therapy over several months, Bortezomib was introduced and resulted in substantial decline in proteinuria leading to persistent complete remission 1.5 years later that was preceded by considerable drop in plasma CD34+, CD105+ and CD138+ cell count, markers of short and long-lived memory plasma cells (Fig. 1). These preliminary observations indicate that B cells play a central role in the immunopathogenesis of RPTMGN involving CD20+ activated B cells and CD20-/CD138+ short and long-lived memory plasma cells belonging to two distinct compartments which consist in the first one (CD20+) of plasmablasts mainly generated in the spleen and lymph nodes and in the second one of short and long-lived memory plasma cells (CD20-/CD138+) found mainly in the bone marrow and the inflamed organ. B cells in both compartments produce auto and alloantibodies in an independent fashion. As expected, short and long-lived memory plasma CD20- cells are refractory to conventional immunosuppressive anti-CD20+ targeting therapy and may be depleted by Bortezomib.

To our knowledge, this is the first case report describing the successful usage of a proteasome inhibitor Bortezomib in RPTMGN refractory to full combined conventional-Rituximab therapy.

Clinical Kidney Histology

BOS533 THERAPEUTIC EFFECTS FOR SUBCLINICAL ACUTE REJECTION IN RENAL TRANSPLANT PROTOCOL BIOPSY

Masaki Muramatsu, Yoji Hyodo, Yoshihiro Itabashi, Hideo Oguchi, Yuko Hamasaki, Hiroshi Nihei, Kei Sakurabayashi, Takeshi Kawamura, Seiichiro Shishido, Ken Sakai, Atsushi Aikawa

Department of Nephrology, Toho University Faculty of Medicine, Japan

Background: Renal transplant biopsy is a golden standard tool to evaluate renal graft. Protocol biopsies is useful to detect morphlogical changes in early stages before clinical signs emerge. The aim of this study reveals therapeutic effects for subclinical acute rejection (AR) based on protocol renal graft biopsies.
Material and methods: We analyzed 268 patients who received a live renal transplant at our center between January 2006 and October 2015. All patients received protocol biopsies at 3 months and 1 year post-transplant. Pathological changes were categorized using the Banff classification. All cases were divided into two groups according to the result of 3 months-protocol biopsies: 213 cases had normal pathological changes (NR) (group A) and 55 cases shown over borderline changes (group B). Group B received anti-rejection therapies such as methylprednisolone and deoxyspergualin. Pathological changes at 1 year post-transplant, graft function (s-Cr) and graft survival were analyzed.
Results: Mismatch of HLA DR in group B was significantly higher than group A ($p = 0.001$, 1.16 $\pm$ 0.06 vs 0.85 $\pm$ 0.64). In the protocol biopsies at 1 year pot-transplant, group A showed NR 173 cases (81.2%), borderline changes (BL) 34 cases (16.0%), >grade 1 (G1) 6 cases (2.8%). Group B presented NR 37 cases (67.3%), BL 9 cases (16.4%), >G1 9 cases (16.4%). In group A, s-Cr (mg/dl) at 3, 6 and 12 months post-transplant were numerically lower than

group B (p = NS, 1.07 ± 0.45, 1.12 ± 0.44, 1.10 ± 0.45 vs 1.20 ± 0.44, 1.19 ± 0.41, 1.2 ± 0.45). In group A, graft survival rates at 1, 3 and 5 years were 100%, 99.4% and 98.5%. Group B also showed excellent graft survival rates (100%, 100% and 100%). There were no statistical differences for graft survival rates between both groups.
Conclusion: Subclinical AR was more likely to be repeated. However, intervention for subclinical AR at early period after transplantation might improve graft prognosis.

Clinical Kidney Immunology

BOS534 ROLE OF SERUM TARGET OF RAPAMYCIN (TOR) AND PERIPHERAL BLOOD NATURAL KILLER CELLS IN PATIENTS WITH RENAL TRANSPLANTATION: RELATION TO ALLOGRAFT FUNCTION AND SURVIVAL

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Background: Mammalian target of rapamycin (mTOR) is a key regulator of cell metabolism, growth and proliferation. The natural killer (NK) cells represent a distinct subset of lymphoid cells that are a key component of the innate immunity. The natural killer T (NKT) cells, constitute a unique lymphocyte population with both T and NK cell surface phenotypic characteristics.
Methods/Materials: This study included 45 subjects; they were divided into three groups each 15, renal transplant patients with stable renal function (Group I), with chronic allograft dysfunction (CAD) (Group II) and healthy subjects as controls (Group III). Measurement of mTOR protein levels was determined using enzyme linked immunosorbant assay (ELISA) kit. The NK and NKT cells in fresh whole blood samples were identified using two-color flow cytometry as $CD3^-CD56^+$ and $CD3^+CD56^+$ cells respectively. Serum creatinine and estimated glomerular filtration rate (eGFR), urinary albumin/urinary creatinine ratio and C-reactive protein (CRP) were done. Renal biopsy was done in patients with CAD
Results: The serum mTOR levels, the percentages of NK cells and NKT cells and serum CRP were significantly higher in both groups of renal transplant recipient compared to healthy subjects. The serum mTOR and NKT cells were significantly higher in patients with Group II than Group I. In patients with renal transplantation serum mTOR levels and both the percentages of $CD3^-CD56^+$ NK cells and $CD3^+CD56^+$ NKT cells in peripheral blood were positively correlated with each other and with serum creatinine, urinary albumin/creatinine ratio, CRP and the degree of renal fibrosis in renal biopsy from patients with CAD.
Conclusions: The dysregulation and activation of mTOR pathway can share in the accompanied stimulation of NK and NKT cells. So, they can play an important role in the pathogenesis and progression of renal injury. Modulation of the mTOR pathway and NK cells could be a potential anti-fibrotic therapy in these patients.

BOS535 SUCCESSFUL RENAL TRANSPLANTATION AFTER DESENSITIZATION IN PATIENTS WITH SENSITIZED END STAGE RENAL DISEASE

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Background: We aimed to evaluate the outcomes of renal transplantation after desensitization in patients with sensitized end stage renal disease.
Materials and methods: We included 44 sensitized patients who were performed desensitization and divided to two groups. Group 1/2: Transplantation (+)/(-) (male/female: 5/7–15/17, mean ages ± SD: 49 ± 11.5/ 39 ± 14.7, p: NS, respectively). The rates of first transplantation before desensitization (7 (58.3%)/ 10 (31.2%), p: 0.164, respectively), erythrocyte transfusion (p: 0.595), pregnancy were similar between groups. Rituximab (375 mg/m^2), immunoglobulin (2 g/kg) and plasmapheresis (30 ml/kg) were used for desensitization. Lymphocyte cross match (LCM) (CDC and Flow Cytometric T/B lymphocyte), panel reactive antibody (PRA) and donor specific antibody were measured before and after desensitization. All these parameters were similar before desensitization, but the rates of LCM positivity were significantly higher in group 2 (p: 0.002), after. LCM were negative in 7 patients and single positive in 5 patients after desensitization. We compared the outcomes of group 1 with 2717 non-sensitized renal transplant patients as subgroup analysis. SPSS 20.0 software program were used for statistical analysis.
Results: Demographic features were similar between group 1 and nonsensitized group. The rates of early and long term graft survival (p: 0.579), patients survival (p: 0.606), acute rejection (16.7%/ 16.5%, p: 0.944), delayed graft function (0/ 19.4%, p: 0.618), chronic allograft dysfunction (0/ 3.2%, p: 0.7), cytomegalovirus (p: 0.853) and BK viremia (p: 0.896), new onset diabetes after transplantation (p: 0.311) and serum creatinine levels (median: mean-max: 1 (0.5–5.2)/ 1.2 (0.1–11.4) mg/dl) were similar between groups.
Conclusion: Our study showed that successful renal transplantation can be done after desensitization by rituximab, immunoglobulin and plasmapheresis in patient with sensitized end stage renal disease.

BOS536 THE INFLUENCE OF PREFORMED HLA CLASS I AND II PANEL REACTIVE ANTIBODIES ON CLINICAL AND PATHOLOGICAL OUTCOMES OF KIDNEY ALLOGRAFT

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Objective: The aim of the study was to investigate the influence of preformed anti-HLA antibodies that are represented by peak PRA levels on clinical and histopathologic outcomes of kidney allograft.
Material and methods: The study was a retrospective cohort that consisted of 111 kidney transplant recipients. A peak PRA level greater than 15% was accepted positive for HLA class I and II antibodies. Flow cytometric assay was used for PRA and lymphocyte cross-match (LCM). All recipients were LCM negative. Allograft biopsies were indication biopsy and evaluated according to Banff 2011 criteria to investigate the influence of HLA antibodies.
Results: PRA was positive in 21.5% of patients for Class-I and 22.5% for Class-II antibodies. PRA Class-II positive patients had significantly more graft failure (p = 0.028), death censored graft failure (p = 0.008), acute rejection (p = 0.016) and chronic rejection (p = 0.029) (Fig. 1). Regarding the pathological evaluation, peritubular capillaritis score was significantly higher in PRA Class-II positive patients (0.44 ± 0.78 vs. 1.55 ± 1.12, p = 0.008) and more patients had a glomerulitis+peritubular capillaritis score ≥2 (64% vs. 36%, p = 0.026). These significant clinical and pathological outcomes were not observed for PRA Class-I and PRA Class I+II positive patients.
Conclusion: Preformed anti-HLA Class-II antibodies are responsible for increased allograft rejection and reduced graft survival despite the negative flow cytometric lymphocyte crossmatch in kidney transplantation.

		ALLOGRAFT LOSS		P value	DEATH CENSORED ALLOGRAFT LOSS		P value
		Yes	No		Yes	No	
PRA CLASS I	Positive	%16.7	%83.3	0.72	%12.6	%87.4	0.98
	Negative	%13.8	%86.2		%12.5	%87.5	
PRA CLASS II	Positive	%28	%72	0.028	%28	%72	0.008
	Negative	%10.5	%89.5		%8.1	%91.9	
PRA CLASS I+II	Positive	%33.3	%66.7	0.12	%33.3	%66.7	0.085
	Negative	%12.7	%87.3		%11	%89	

Clinical Kidney Rejection

BOS537 LONG-TERM RESULTS OF A CASE OF ABO INCOMPATIBLE KIDNEY TRANSPLANTATION WITH HIGH TITER OF ANTI-ABO ANTIBODY USING ECULIZUMAB INDUCTION

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Several reports described that the result of ABO incompatible kidney transplantation (ABOiKT) with very high titer of anti-blood type antibody was

not good. We were performed successfully ABOiKT with pre-operative high anti-blood type antibody titer using eculizumab induction.

A 29-year-old female, blood type O, was scheduled to receive ABO-blood type incompatible kidney from her father, blood type A. Her baseline anti-blood type A IgG and IgM antibody titer were 4096× and 512×, respectively. Our induction protocol for ABOiKT consisted of tacrolimus, mycophenolate mofetil and steroid starting from 45 days prior transplantation in combination with two times of anti-CD20 antibody injection (day −45 and −30) and 3 sessions of double filtration plasmapheresis (DFPP).

However, anti-blood type A antibody titer did not lower and IgG and IgM were still 1024× and 128×, respectively. Six sessions of IVIg (total 160 g/body) with 5 sessions of plasma-exchange (PEX) were added after DFPP. Her anti-blood type A IgG and IgM antibody titer were gradually decreased and lowered to 32× and 8×, respectively on the day of kidney transplantation. Because the patient was considered to be an immunologically high risk recipient with a high titer of the anti- A blood type antibody and the titer did not lower even after the rigorous treatment including many times of PEX and IVIg, a series of eculizumab (900 mg weekly 5 times and biweekly 3 times) treatment was given for this patient.

After kidney transplantation, a biopsy specimen obtained on postoperative day 14 showed no evidence of rejection with good renal function (serum creatinine, 1.5 mg/dl). However, the patient showed signs of antibody-mediated rejection which was confirmed by biopsy after 6 months, and was treated successfully with steroid pulse therapy and IVIg.

Eculizumab could be an effective treatment option for the ABO-incompatible kidney transplant patient with a high anti-blood type antibody titer.

BOS538 A NEW PAIRED KIDNEY DONATION (PKD) STRATEGY FOR VERY HIGHLY SENSITIZED PATIENTS (VHSP): A SINGLE CENTER EXPERIENCE

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Introduction: Kidney Transplantation of VHSP (defined as HLA sensitized patient with calculated PRA of ≥98%) remains a daunting task in all reported single center and national PKD registries. We sought to explore a new strategy to facilitate transplantation of VHSP via single center PKD program.

Methods: In May 2016, we established a new PKD program at our center utilizing Biologic Tx Matchgrid software. In addition to listing of HLA and ABO incompatible (HLA I and ABO I) pairs, the key features of our new strategy consist of the following:

- Listing of compatible pairs (CP) with poor HLA match, defined as ≥6 HLA mismatches with the original donor (HLA A, B, DR, DQ matching scheme). The aim is to provide CP with age and size matched but better HLA class II matched exchange donor (balanced altruism).
- A qualified breach of ABO and/or HLA barrier with the exchange donor via desensitization is allowed for VHSP, provided that the antibody titer is low.

Results: As of March 2017, and from an average PKD pool size of 100 pairs, thirty three (33) LD kidney transplantations were performed via PKD. 11/33 (33%) were VHSP. They were all females and their average age was 50 (range: 26–61) years. 8/11 (72%) VHSP were desensitized for breaching the HLA/ABO barrier with their exchange donors. As such, PKD for VHSP yielded kidney transplantation with an average HLA class II (DR and DQ) antigen mismatches/matches of 1.4/2 (range: 0–4) with the exchange donor. Over an average follow-up of 123 (range: 7–244) days, Patient survival was 100%, Graft survival was 100%, and average serum creatinine was 77 (range: 67–90) μmol/liter. Incidence of AMR was 0% and incidence of ACR was 18% (2/11 patients developed Banff II A rejections which were totally reversed with treatment).

Conclusion: A PKD strategy consisting of balanced altruism for CP and a qualified breach via desensitization of ABO/HLA barriers with the exchange donor in VHSP was successful in granting VHSP quality kidney transplantation.

BOS539 RETROACTIVE APPLICATION OF A NEW RISK INDEX FOR LIVING DONOR KIDNEY TRANSPLANTATION (LKDPI) TO RENAL TRANSPLANTS IN VERACRUZ, MEXICO

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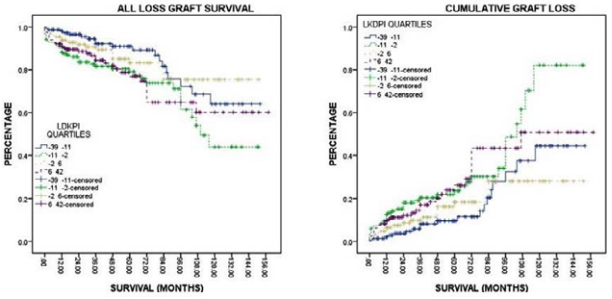
Imss Umae 14 Adolfo Ruiz Cortines, Mexico

Background: Kidney Donor Profile Index (KDPI) was designed to estimate the graft loss risk in deceased donor transplants. Recently, the Epidemiology Research Group for Organ Transplantation created the living donor kidney profile (LDKPI). This model predicts recipient risk of graft loss after living donor transplant on the same scale as the KDPI. Herein, we applied the LDKPI to our population to analyze its performance.

Methods: Retrospective analysis of all living donor kidney transplants from 2003 to 2015 from two transplant centers in Veracruz, Mexico. LKDPI was calculated in a web-page (www.transplantmodels.com) Donor/Recipient demographics and transplant data included in the model were registered. Pearson correlation between LKDPI percentage and survival was performed. Kaplan–Meier survival (log-rank) and Cox regression analysis was compared between LKPDI quartiles. $p < 0.05$ was considered statistically significant.

Donor and Recipient Characteristics	Results (n = 605)
Donor age: years ± SD (range)	38.9 ± 9.6 (18–65)
Donor sex: male/female (%)	275 (45.5) / 330 (54.5)
Recipient sex: male/female (%)	368 (60.8) / 237 (39.2)
Donor eGFR: ml/min ± SD (range)	104.08 ± 18.05 (59.9–156)
Donor SBP: mmHg ± SD (range)	111.7 ± 12.2 (80–160)
Donor BMI: kg/m^2 ± SD (range)	24.6 ± 3.6 (16.1–38)
Donor African American: No (%)	100%
Donor History of Cigarette use: Yes (%)	1 (0.2)
Donor/Recipient Biologically related: Yes (%)	448 (74)
Donor/Recipient ABO incompatible: NO (%)	100%
Donor/Recipient weight ratio: n ± SD (range)	0.88 ± 0.04 (0.5–0.9)
Donor/Recipient HLA-B one mismatch: N (%)	375 (62)
Donor/Recipient HLA-DR one mismatch: N (%)	413 (68.3)

Figure 1. Graft loss in kidney transplant recipients by LKPDI quartiles



Results: 605 transplants were included. Table 1 (Fig. 1) displays donor/recipient data for LKDPI calculator.

Conclusion: Mean LKDPI was − 2.32 ± 13.6 (−39 to 42 range). Pearson coefficient correlation between LKPI and graft survival was −0.82 (95% IC −0.165 to −0.001) (p = 0.044). Recipients with the lowest LKDPI had lower risk of 1 and 5 year graft loss than other quartiles (p = 0.012 log rank) (Figs 1 and 2). Cox regression analysis was significant for lower LKDPI quartile (−39 to −11) (p = 0.027, Exp B = 0.258 95% CI, 0.300–0.929)

LKPI confidently applies in cumulative graft loss during first 5 years of kidney transplant. Longer survival might be influenced by other factors in our population.

BOS540 INCIDENCE OF POST KIDNEY TRANSPLANT NEUTROPENIA IN CHILDREN AND THE IMPACT OF MYCOPHENOLATE MOFETIL DOSE REDUCTION ON THE INCIDENCE OF REJECTION AND GRAFT SURVIVAL

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Background: Neutropenia following pediatric kidney transplant is not uncommon problem. In attempts to reduce the incidence of severe bacterial infection, mycophenolate (MMF) dose is frequently reduced. In this study, we hypothesize that MMF dose reduction in the early post-transplant period is associated with higher incidence of graft rejection and worse short term graft function.

Methods: This is a single center, retrospective cohort of 75 pediatric patients under 17 years of age who underwent kidney transplantation from August 2008 to December 2015. All absolute neutrophil counts (ANC) were collected until 1 year post transplant. The lowest ANC was documented and all episodes of MMF reduction in the first year of transplantation were collected. The risk of neutropenia was calculated using multivariate logistic regression and the risk of acute rejection was predicted using multivariate cox regression.

Results: Majority of patients (90.7%, *n* = 75) had at least one episode of neutropenia (ANC< 2000), 16 of whom (21.3%) had severe neutropenia (ANC< 500). Median time to neutropenia was 101. There were 7 episodes of bacteremia requiring IV antibiotics, of which only one episode was associated with severe neutropenia. Grade of neutropenia did not correlate with the risk of infection (p = 0.94). MMF dose was the only independent risk factor for neutropenia development (adjusted OR = 1, p = <0.0001, 95% CI = 0.004–0.0015). The incidence of acute rejection was significantly associated with the cumulative duration of MMF dose reduction (adjusted HR 1.006, p = 0.019, 95% CI = 0.001–0.01). No difference in 1 year (mean eGFR 91.52 vs. 92.0 p = 0.977) and 3 years (mean eGFR 70.68 vs. 86.91 p = 0.168) graft function in patients with and without MMF reduction.
Conclusion: in spite the high incidence of neutropenia observed, severe infection was not common. MMF dose reduction in the first year of transplant was associated with an increased risk of graft rejection but not with worse short term graft function.

BOS541 EXTRACORPOREAL PHOTOPHERESIS AS INDUCTOR OF PARTIAL IMMUNOLOGICAL TOLERANCE IN RENAL TRANSPLANTATION

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Extracorporeal photopheresis (ECP) is an effective method of resistant transplant rejection management. This method is widely used in renal, heart, and lung transplantation. In terms of renal transplant rejection prevention this method and its mechanism of action is not studied well enough.
Purpose: To study both the mechanism of action of ECP and its influence on frequency of rejection episodes and renal transplant function.
Materials and methods: A prospective randomized study in 24 pairs of recipients has been conducted. One donor kidney was transplanted to a patient of the main group, the other – to the patient of the control group. The main group patients was treated with 15 sessions of ECP.
A percent (%) of naïve T-helpers expressing CD28 (CD3+CD4+CD27+CD28+CD45RO– phenotype) and mean fluorescence index (MFI) of the molecule were investigated.
Results: In healthy people CD28 is present on the whole surface of naïve T-helpers pool. However, its MFI is greatly variable.
In recipients of renal transplant on 4th day after transplantation CD28 + Th and MFI decrease significantly – p < 0.001. In the main group on 30th day a significant decrease in percent of CD28 + Th (p < 0.001) and MFI (p < 0.001) was observed in relation to the parameters on 4th day after transplantation. This dynamics in patients of the main group can be indicative of a specific and universal inhibition of expression of co-activating molecules on naïve T-helpers.
Patients in control group on 30th day after transplantation had no significant changes in percent of T-helpers expressing CD28 (p = 0.42), and MFI (p = 0.087).
The number of CD28 + Th in patients of the main group was statistically different from that of control group (p < 0.001).
Also in the main group the number of CD8 cells on 30th day was significantly lower than that on 4th day (p = 0.02), as well as in control group (p < 0.001).
ECP is an inductor of partial immunological tolerance to transplant. The study assessing long-term outcomes is in progress.

Clinical Kidney Histology

BOS542 SUCCESSFUL TRANSPLANTATION OF ECD DCD KIDNEYS USING REMUZZI SCORING TO DIFFERENTIATE BETWEEN SINGLE AND DUAL TRANSPLANTS

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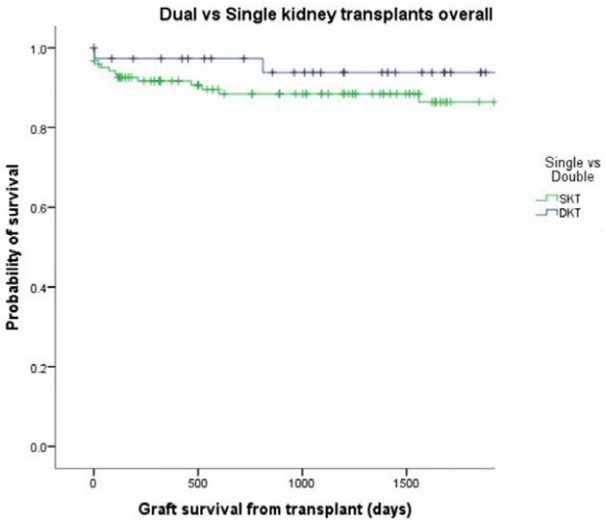
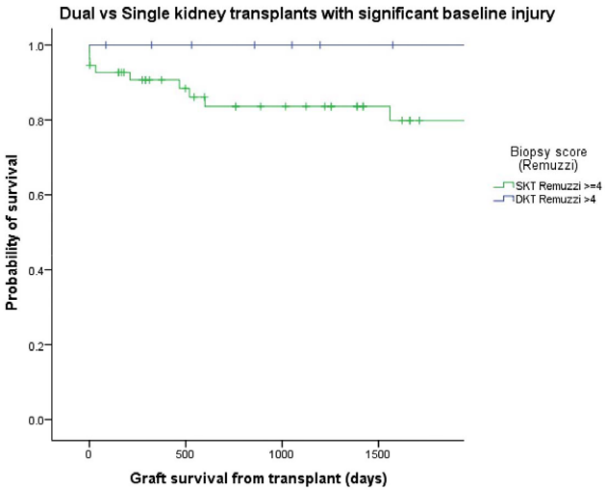
Background: Expanded criteria circulatory death donors (DCD) are a frequently not pursued and may represent an underutilised donor pool. Our centre has used urgent pre-implantation biopsy (Remuzzi score) to guide single (SKT) vs. dual (DKT) kidney transplantation: here we report outcomes for a cohort of predominantly DCD donors over 65.
Methods: DCD kidney only transplants from donors over 65 performed between 2009 and 2016 (*n* = 39 DKT, *n* = 123 SKT) were identified from a prospectively maintained database. One, three and five year eGFR and death censored graft survival was compared for single and dual transplants.
Results: Despite more severe baseline injury (Remuzzi scores 4.3 vs. 3.4, p < 0.001), higher rates of hypertension (69% vs. 46%, p = 0.013) and diabetes (18% vs. 7%, p = 0.049) DKTs provided better death censored graft survival at 5 years (94% vs. 86%, Fig. 1) with significantly better 1 and 3 year





eGFR (47.5ml/min vs. 36.9ml/min, p = 0.003; 53.6ml/min vs. 42.53ml/min, p = 0.041) compared to SKTs from donors with otherwise similar clinical characteristics (Fig. 1) [GP1]. This difference in survival was most marked for kidneys with moderately severe (Remuzzi score >4) baseline injury; whose 5-year survival was 100% when implanted as a dual transplant, but only 80% when implanted singly (Fig. 2). In contrast, no difference in survival was observed between dual and single transplantation for kidneys with favourable (<4) Remuzzi scores (5 years survival dual 91% vs. single 93%).
Conclusion: Our results indicate that ECD DCD kidneys can be transplanted safely and suggest that the use of preimplantation biopsy analysis to guide single or dual transplants helps mitigate the risk of early graft failure.

Clinical Kidney Surgical Technique

BOS544 SEARCH FOR THE MOST DEVELOPED LAPAROSCOPIC DONOR NEPHRECTOMY

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Donor nephrectomy is a surgery for a healthy person. It should be less invasive and the laparoscopic surgery is principally employed as the donor nephrectomy. Three new different laparoscopic donor nephrectomies were evaluated to search a superior method comparing with our standard one with 3 ports (12 mm diameter port) and 5 cm incision at lower abdomen for the left side (LAP).

Fifteen cases of laparoscopic single port nephrectomy with 5 cm navel incision (LESS), eight cases of laparoscopic single port nephrectomy with 2.5 cm navel incision and additional suprapubic 5 cm incision (LESS+Ph) and Reduced port laparoscopic donor nephrectomy with 2 ports (3 mm and 5 mm ports) and superpubic 5 cm incision (RPS) were evaluated to the LAP group (15 cases). The left side cases were selected to evaluate and all operations were performed by one expert surgeon.

The each mean operating time was 225.1 min of LAP, 274.3 min of LESS, 234.5 min of LESS+Ph and 185.6 min of RPS. The each warm ischemic time was 227.5 sec, 227.4 sec., 214.8 sec. And 212.7 sec. Additional analgesic after the operation was 1.1 times, 0.6 times, 0.6 times and 0. Admission period after the operation was 7.4, 5.3, 6.0 and 5.0 days. There was no operative complication in all operations. LESS-Ph and RPS were superior on the cosmesis.

RPS would be concluded as the most developed laparoscopic donor nephrectomy from less invasive factors, cosmesis and also reasonable difficulty of the manipulation linked to safety.

BOS545 INCREASED WARM ISCHEMIA TIME WITH LAPAROSCOPIC LIVING DONOR NEPHRECTOMY: MYTH OR REALITY?

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Introduction: Laparoscopic donor nephrectomy (LDN) is generally considered a better option than open donor nephrectomy (ODN) in renal transplantation associated with better cosmetic results, lesser post-operative pain, and faster recovery. LDN has a longer learning curve and was associated with increased operative time and warm ischemia time when compared with ODN. Herein we compare mini-incision donor nephrectomy (MDN) with LDN approach regarding short- and long-term outcomes.
Methods: Two hundred and fifty one patients, who underwent donor nephrectomy using MDN ($n = 141$) and LDN ($n = 110$), performed by the same surgical team, were compared with respect to operative time, warm ischemia time, complications and hospital stay. Graft function was evaluated on the short-term considering Acute Tubular Necrosis (ATN) episodes during the first week and Delayed Graft Function. Long-term outcomes were assessed by Serum Creatinine (SCr) and Glomerular Filtration Rate (GFR) through the first year after transplantation.
Results: The mean operative time for MDN (120 $\pm$ 29 min) was not significantly different when compared to LDN (127 $\pm$ 32 min, $p = 0.08$). Laparoscopic donors had a shorter warm ischemia time (238 vs. 310 s, $p = 0.01$), hospital stay (4.3 vs. 5.9 days, $p < 0.001$) and postoperative complications ($p = 0.03$). The incidence of graft ATN was superior in the MDN (89 vs. 25%, $p < 0.001$) without significant difference regarding the long-term outcomes (first year SCr 1.38 vs. 1.33 mg/dl, $p = 0.7$ and first year GFR 63.7 vs. 63.1 ml/m^2, $p = 0.9$).
Conclusion: Opposing the most recent meta-analyses we had shorter warm ischemia times in laparoscopic comparing with the open nephrectomies without increasing the duration of procedure. With the growing experience in high volume centres with specialized teams, LDN could be considered the most suitable technique for living donor nephrectomy with significantly better results in the short-term, without difference in long-term outcomes.

BOS546 3D ENDOSCOPIC DONOR NEPHRECTOMY VS. ROBOT-ASSISTED DONOR NEPHRECTOMY: A DETAILED COMPARISON OF TWO PROSPECTIVE COHORTS

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Background: Visual misperception, an important cause of surgical accidents, could be overcome by restoring three-dimensional (3D) view during endoscopic procedures. There are two surgical techniques that implement 3D vision: 3D endoscopy and the robotic surgical system. We aimed to assess whether 3D endoscopy during living donor nephrectomy (LDN) is safe for donors and feasible for the surgeon.
Methods: We prospectively collected data on consecutive patients undergoing 3D endoscopic LDNs in a single center in the Netherlands. Donors' pre-, intra- and post-operational data were collected, as well as recipient and graft survival, with the endpoint 90 days after surgery. These data were compared to robot-assisted donor nephrectomies (RADNs) in our center. A questionnaire was used to assess surgeon's experience.
Results: Forty 3D endoscopic procedures were performed from April 2015 to April 2016 by two robot-certified surgeons. Baseline characteristics were comparable, with 26 vs. 24 females, a median age of 58.0 (26.0–78.0) vs. 54.0 (19.0–76.0) and BMI of 26.1 (19.9–40.4) vs. 23.8 (17.9–38.0), for the 3D endoscopic and RADN group respectively. Three-months post-operative outcomes demonstrated no significant differences for donors, nor recipient and graft survival. Intraoperative results showed a significantly shorter median skin-to-skin time, 138.5 min (85.0–231.0) vs. 167.0 (110.0–266.0) minutes ($p = 0.001$), in favor of the 3D group. Questionnaires showed that both surgeons felt comfortable, especially when encountering the renal vessels (hilar phase), with a significantly shorter hilar phase for both single- and multiple anatomies ($p = 0.009$ and $p = 0.040$, respectively).
Conclusion: 3D endoscopy for donor nephrectomy is feasible for surgeons and safe for the donor. In addition, there were no differences in recipients' or transplant outcomes. The duration of 3D endoscopy was significantly shorter, as well as the hilar phase.

BOS547 LIVING DONOR NEPHRECTOMY: FROM HAND ASSISTED TO SINGLE PORT

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Introduction: There are multiple laparoscopic surgical techniques for living donor nephrectomy which are now standard practice. The clinical outcomes appear comparable but the transition from one surgical approach to another has not been widely explored. We investigated the outcomes of three different surgical techniques in a single centre experience and assessed the ease of change in clinical practice.
Methods: 201 patients underwent donor nephrectomy between 2009 and 2016. Socio-demographic and comorbidity data as well as biochemical investigations, assessment of renal function, operative data (type of surgery, duration, blood loss, warm ischemic time, vascular anatomy), postoperative hospital stay, pain relief utilisation, renal function recovery and complications (Clavien scoring) were analysed. Post-operative donor renal function was assessed using MDRD equation daily during hospital stay, at 6 weeks and 12 months post-operatively
Results: 48 patients underwent hand assisted laparoscopic procedure (HALDN), 88 total laparoscopic (LN) and 65 Single port (SILS) nephrectomy. There were no differences in donor demographics, pre-donation renal function and vascular anatomy (Table 1). SILS operative duration was 30 min shorter compared with LN. The number of patients developing Clavien grade 2–3 complications was comparable between all three techniques ($p = 0.202$). SILS was associated with the shortest post-operative stay compared with the other two methods (4.7 days vs. 5.1 for HALDN vs. 5.89 for LN). SILS patients required less post-operative pain relief medication compared with the other two techniques and had a quicker recovery of renal function post-donation.
Conclusion: The transition from LN and HALDN to SILS is smooth and can be easily implemented with previous experience of laparoscopic nephrectomy. SILS appears to provide a better post-operative recovery and shorter hospital stay.

	SILS ($n = 65$)	HALDN ($n = 48$)	LN ($n = 88$)	p-value
Age (median)	52	53	49	0.504
Gender (M:F)	35:30	21:27	48:40	0.967
Number of arteries [Median (range)]	1 (1–3)	1 (1–3)	1 (1–3)	1.576
Median BMI (kg/m^2) (range)	25.5 (18, 32)	26.08 (20, 36)	26 (17, 34)	2.00
Median eGFR (ml/min/ 1.73 m^2) (range)	91.0 (70, 160)	90.0 (71, 124)	98.0 (74, 137)	1.616
Median split function R kidney (range)	49.0 (42, 60)	47.5 (39, 56)	50.0 (45, 57)	0.704
Median operative duration (min)	172.50	185	199.50	0.299

BOS548 AORTO-BISILIAC BYPASS USING A VENOUS HOMOGRAFT AND CONCOMITANT KIDNEY TRANSPLANTATION IN A PATIENT WITH SEVERE BILATERAL ILIAC OCCLUSIVE DISEASE: REPORT OF A CASE

Elia Zani[1], Giuseppe Ietto[1], Gabriele Soldini[1], Domenico Iovino[1], Cristiano Parise[1], Veronica Raveglia[1], Marco Calussi[1], Matteo Tozzi[2], Giulio Carcano[1]

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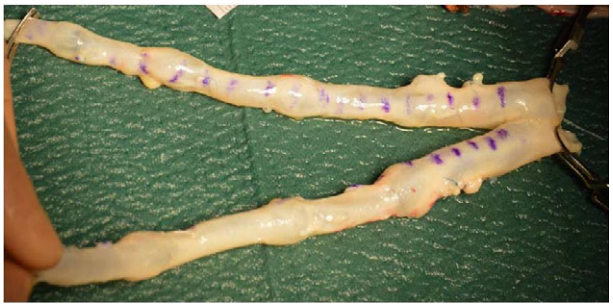
Background: Increasing age of transplant recipient leads to a higher incidence of arterial disease; aortoiliac occlusive disease (AOD) is a great threat for kidney transplantation (KT) and usually considered as a major contraindication. Here we report the case of an aortoiliac bypass, performed simultaneously with renal transplantation, using vascular grafts obtained from the same dead donor of the kidney.
Materials: The recipient was a 68 years old woman with significant stenosis of the aortoiliac axis. The donor was a 50 year old male with methicillin resistant S. Aureus haemoculture positivity that contraindicated a prosthesis implant on the recipient; we decided to harvest also donor's superficial femoral veins. During backtable reconstruction a pantaloon anastomosis was crafted between the two venous grafts and the so obtained homograft was employed to perform an aorto-bisiliac bypass. KT was then carried out using a standard technique. A terminolateral arterial anastomosis was crafted between the graft renal artery and the right branch of the aortoiliac graft. Operative time amounted to 330 min and cold Ischemia time of the renal graft was 900 min. Delayed graft function (DGF) was observed until postoperative day (POD) 12. Postoperative renal doppler ultrasonography showed a good renal perfusion with mildly augmented resistive index. Discharge was on POD 30 in good clinical state with normal urine output and a serum creatinine of 2.1 mg/dl.

Discussion: Performing transplantation after insertion of a vascular prosthetic graft increase operative time and graft's cold ischemia. Good return to function after initial DGF suggest that, such intervention, allows transplantation to be offered to those patients before excluded for severe vascular comorbidities. The employ of homologous vascular grafts is a good choice because prosthetic vascular replacement during immunosuppression must be avoided as long as possible, especially with coexisting infective risk.



BOS549 HAND-ASSISTED EXTRAPERITONEOSCOPIC LIVE-DONOR NEPHRECTOMY: SINGLE CENTRE EXPERIENCE SINCE 2011: 250 CASES

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Background: Our study reports last 250 consecutive hand assisted retroperitoneoscopic live donor nephrectomies (HARS) performed at our institution since 6/2011 till 7/2016. HARS nephrectomy technique has been introduced by the author in Prague/Czech Republic in January 2003, since June 2011 is being used for all the donors including right sided and complex anatomy cases (multiple vessels and ureters, retroaortic renal vein, renal artery diseases, etc). The main benefit of HARS approach is increased safety for the donor. Risk of bleeding and intraabdominal injury is low thanks to hand assistance and extraperitoneal approach.
Methods: Data were collected prospectively. The operation is performed in the manner described by Wadström 2002, with minor modifications. There were all anatomical variations accepted for surgery, including right sided cases when indicated.
Results: There was no conversion to open nephrectomy. The median blood loss was zero, meaning no use of suction or no blood in container. The median post-operative hospital stay was 2 days. We observed few minor complications including one wound infection, five wound seromas and three wound haematomas. Mean donor age was 48 years (19–73, min–max). Average WIT was 102 s (SD 32). Mean operating time was 120 min (SD 35 min). There were 45% of kidneys with complex anatomy. Retroaortic renal vein was in 14% of nephrectomies. There was one case of postoperative bleeding from paraaortic lymphatics which required retroperitoneoscopic re-operation, there was one case of incisional hernia which occured some 8 months after surgery. All donors have life-long follow up.
Conclusions: HARS is a safe way of performing living-donor nephrectomy with low risk of severe complications, minimal morbidity and fast recovery. It is safe alternative to the transperitoneal mini-invasive as well as other nephrectomy techniques. It can be used safely for all the anatomical variations as well as right sided cases.

BOS550 IMPROVING THE QUALITY OF DONATED KIDNEY: LEFT MULTIPLE-ARTERY VS. RIGHT SINGLE-ARTERY KIDNEY DONATION

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Preserving the best kidney for the donor is the key of living donation. Due to the shorter renal vein, increasing the incidence of venous thrombosis in right allografts, left kidneys are frequently elected. However, left arterial anatomy may be complex, rendering the transplantation demanding. Analysing outcomes after left multiple-artery kidney (LMAK) and right single-artery (RSAK) nephrectomy could aid in decision-making.

Fifty-six cases: 28 LMAK (14 open, 14 lap) and 27 RSAK (13 open, 14 lap) nephrectomies were compared. Graft function was evaluated in the short-term considering Acute Tubular Necrosis (ATN) episodes in the first week and Delayed Graft Function. Long-term outcomes were assessed by Serum Creatinine (SCr) and Glomerular Filtration Rate (GFR) through the first year after transplantation.

There were no difference in mean operative time between LMAK (140 $\pm$ 32 min) and RSAK (127 $\pm$ 36 min), warm ischemia time (264 $\pm$ 179 vs. 211 $\pm$ 72 s), donor hospital stay (5.0 $\pm$ 2.5 vs. 4.6 $\pm$ 1.1 days), receptor hospital stay (12.1 $\pm$ 9.6 vs. 13.0 $\pm$ 6.9 days) and post-operative complications ($p = 0.76$). Comparing open and laparoscopic procedures there were also no difference between the groups. ATN was superior in RSAK (67 vs. 39% $p = 0.01$) although there were no significant difference in the SCr and GFR through the first year of transplantation. Mean first year SCr in LMAK receptors was 1.3 mg/dl vs. 1.4 mg/dl in RSAK ($p = 0.4$) and GFR was 77 ml/m^2 in LMAK vs. 75 ml/m^2 in RSAK receptors ($p = 0.7$). There were 2 cases of vein thrombosis in RSAK with graft loss and no cases of arterial thrombosis.

This is the first study comparing LMAK with RSAK living donor nephrectomies. Herein we can conclude that the safety and efficacy of LMAK do not differ. Moreover we recorded two cases of renal vein thrombosis after RSAK transplantation without any increment in cases of arterial thrombosis in LMAK. Despite being technically more difficult LMAK could be a good option for living donation expanding the donor pool.

BOS551 COMPARISON OF LAPAROSCOPIC SINGLE-SITE DONOR NEPHRECTOMY WITH OPEN EXTRACTION OR VAGINAL EXTRACTION TECHNIQUES – A SINGLE CENTER EXPERIENCE

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Backgrounds: The aim of this study is to compare the results of single-site laparoendoscopic donor nephrectomy with open extraction (LESSDN-OE) and vaginal extraction (LESSDN-VE).
Methods/Materials: We analysed the data of 18 female donors who underwent LESSDN-OE (Group I: 9) and LESSDN-VE (Group II: 9) in our center. All donors had one renal artery and vein. Parameters regarding donor age, body mass index (BMI), length of hospitalization, duration of surgical procedure, amount of blood loss, warm and cold ischemia times, side of graft nephrectomy, averages for postoperative (PO) visual analogue pain scores at 0th and 1st days (VAS-0, VAS-1), peri-and PO complications of donors, averages of PO fever at 1 h and 2nd days, averages of PO arterial oxygen saturation at 0 h and 1st days, graft function at discharge and PO sixth month were compared between two groups statistically with Mann-Whitney U test.
Results: All of the donors in both groups had left sided nephrectomy except two in Group I. No significant difference in terms of donor age, BMI, mean operative time, amount of blood loss, length of hospitalization, warm ischemia time, VAS-0, PO fever and oxygen saturation was observed between two groups. However, cold ischemia time was lower in Group I ($Z = 3.13$, $p < 0.01$) and VAS-1 was lower in Group I ($Z = 1.98$, $p < 0.05$). No perioperative complications occured for donors and recipients in both groups. In both groups, two donors presented with fever higher than 38 degrees of centigrade due to PO atelectasis at first PO day. An acute rejection episode which was treated successfully occured for two recipients of Group II in first six mount after

transplantation. Graft function at discharge and graft survival at PO sixth month were similar in both groups.
Conclusion: Since our first priority is to minimize the morbidity of donors, LESSDN-VE can be chosen in selected female donors not only for better cosmetic outcomes but also similar graft survival rate as seen in LESSDN-OE.

BOS552 VASCULAR RECONSTRUCTION IN KIDNEY TRANSPLANTATION

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Background: The number of transplantation increases every year. However, the average waiting time for organ transplantation remains up to 5–6 years in European countries. Therefore, the possibility to use organs with vascular abnormalities and performing various techniques of kidney vessels reconstruction remain the topical issue.
Material and methods: We analyzed 301 patients after kidney transplantation. There were 90 (29.9%) patients (females 38, 41.7 ± 11.7 years, and males 52, 37.5 ± 11.1 years) with vascular reconstruction of kidney allograft (total 94). Cadaveric donor transplantation was performed in 81 (90%) patients and in 9 (10%) cases – living related kidney transplantation. To evaluate the perfusion after renal transplantation it was used the color duplex sonography.

There were 77 (81.9%) reconstructions of the renal veins and 17 (18.1%) – of the renal artery. Veins reconstruction included: vein elongation by using the cadaveric donor vein cava inferior in 73 (77.6%) cases, elongation by using superficial vein (living donors vein) in 2 (2.1%), in one case (1.1%) elongation by using PTFE and the formation of a common venous mouth in 1 (1.3%) patient.

Basically, arterial reconstructions were consisted of the common arterial neo-ostium formation in 10 (10.6%) cases, elongation of the renal artery – 6 (6.4%) and in one case (1.1%) it was plastic of kidney artery stenosis allograft by the PTFE.
Results: During the follow up period 1.2 ± 0.6 years there weren't any vascular complications. The color duplex sonography results on the 14 ± 2.6 days after operation show the artery peak systolic flow velocity – 85.2 ± 29.8 cm/s, the average local rate of blood flow in the veins – 41.9 ± 14.9 cm/s. The average resistance index was 0.7 ± 0.1.
Conclusions: The adequacy of blood supply in the allograft is one of the main factors of vitality and function of kidney and the effectiveness of transplantation itself. This study showed good result.

BOS553 RENAL ARTERY ANEURYSM REPAIR USING LAPAROSCOPIC NEPHRECTOMY, BACK BENCH VASCULAR RECONSTRUCTION AND AUTOTRANSPLANTATION: CASE SERIES OF 6 SURGICAL PROCEDURES

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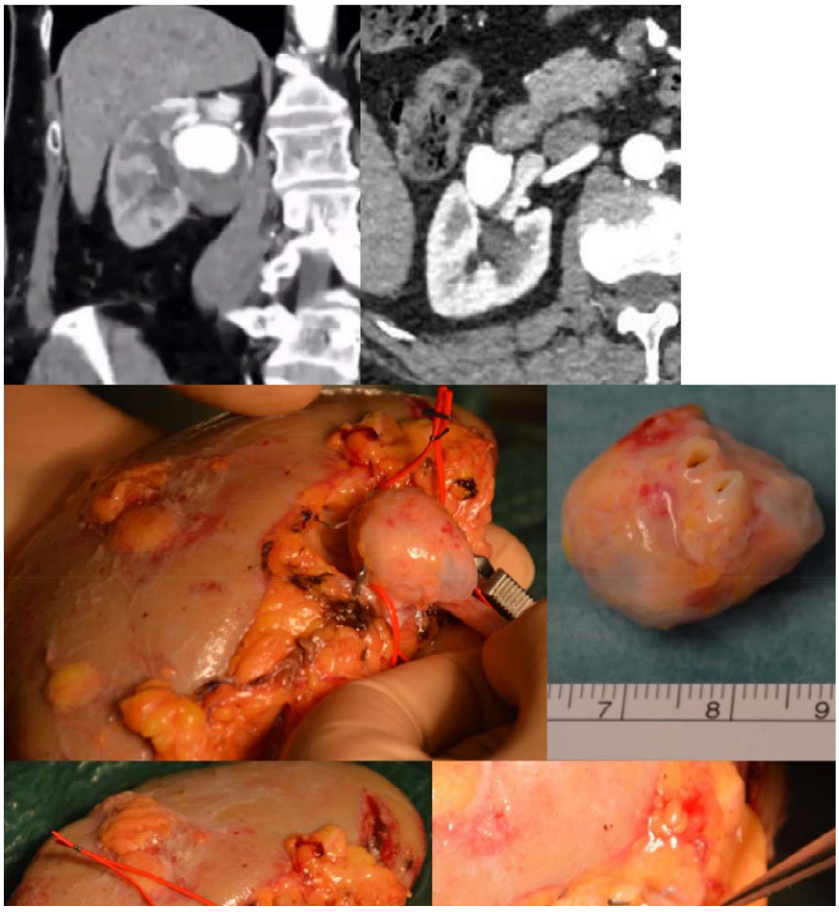
Background: Operative repair of renal artery aneurysm (RAA) may be accomplished by different techniques; actually, endovascular stent-grafting or embolization procedures are an attractive alternative for the RAAs treatment. However, RAA beyond the renal artery bifurcation may require an open treatment with in vivo or ex vivo surgical repair.
Materials/Methods: In the period between February 2013 and June 2016 we observed 6 patients with renal artery aneurysmal disease. All patients had complex renal artery aneurysm and was placed indication for surgical treatment characterized by laparoscopic nephrectomy, back bench vascular reconstruction ex vivo with or without autologous tissue (gonadal vein) followed by autotransplantation in the iliac fossa. In all 6 cases it was possible to perform aneurysmectomy and vascular reconstruction of the renal artery at the bench. In 2 cases the reconstruction after aneurysmectomy occurred by direct suture or direct anastomosis between the arterial branches. In 4 cases it was necessary to use patches or gonadal vein grafts The reconstruction time at the bench was between 120 and 335 min with an average of 249 min, depending on the complexity of the vascular reconstruction. All patients underwent seriated controls of the serum creatinine values. During the postoperative course we were also collected ultrasound data and MRI angiography. The average follow up time was 20 months.



Results: In our casuistry of 6 patients treated in all cases we observed a normalization or an optimal preservation of renal function during the follow-up and in no case there were major complications.
Conclusion: Surgical treatment of complex renal artery aneurysms using laparoscopic nephrectomy, vascular reconstruction at the bench and auto-transplantation is a surgical technique that provides satisfactory results in terms of safety, morbidity and short-middle term renal function.

BOS554 AN ALTERNATIVE APPROACH FOR KIDNEY TRANSPLANTATION TO SPLENIC VESSELS IN PATIENT WITH OCCLUSIVE INFERIOR VENA CAVA (IVC)

Sigal Aizner[1], Michael Gurevich[1], Eviatar Nesher[1], Vadym Mezhybovsky[1], Vladimir Tanek[1], Eytan Mor[2]
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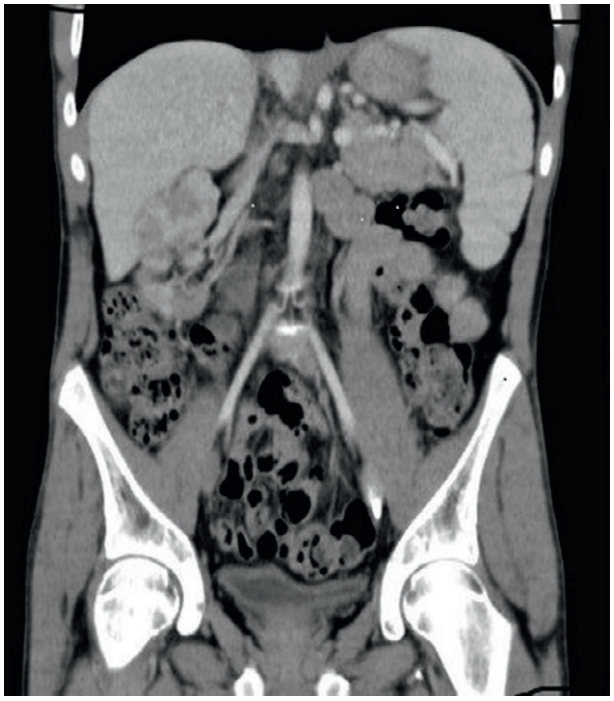
In case of IVC thrombosis or other occlusive anomaly renal transplantation might be challenging. One solution in these patients is splenectomy and anastomosis of renal vessels to splenic artery and vein. Until now, only a few cases were published describing this surgical technique.

Our patient is a 27 years old with dysplastic kidneys and vesico-ureteral reflux leading to ESRD during childhood. The first live donor renal transplant was performed at age of 7 yr. from his mother. The renal graft was placed at right iliac fossa and connected to iliac vessels. The surgery was complicated by renal artery thrombosis and the graft was removed on POD-2. A month later the patient was re transplanted with a cadaveric kidney. Due to the finding of atretic IVC from the level of the renal veins down to iliac veins, the graft's renal vein and artery were anastomosed to the infra-hepatic IVC, and to the aorta, respectively. This graft lasted for 18 years and the patient returned to dialysis. In pre-transplant evaluation for relisting there was no patent IVC for anastomosis which enforced us using the splenic vessels after a total splenectomy. The patient received a prophylactic vaccination and following 3 years of waiting a deceased donor graft was offered.

In surgery a total splenectomy with dissection of a long splenic artery and vein was carried out. The kidney was placed in the LUQ with an end-to-end anastomosis to the splenic vessels. The ureteral anastomosis consisted of an end- to-side anastomosis between the grafts to native ureter after double J-stent insertion. The immediate graft function was normal with an excellent arterial and venous flows on Doppler US. The serum creatinine rapidly decreased to normal value. During the 1-year follow up the patient remained with normal graft function. We conclude that for patients with veno-occlusive anomaly of the IVC splenectomy and anastomosis to splenic vessels is a doable and safe solution for renal transplantation.



BOS555 IS ULTRASOUND GUIDED PERCUTANEOUS RENAL BIOPSY SAFE IN ROBOT ASSISTED KIDNEY TRANSPLANT PATIENTS?

Fatih Gokhan Akbay[1], Aysegul Kudu[1], Aysun Erbahceci Sali[2], Filiz Islim[2], Mesude Yasemin Ozluk[3], Isin Kilicaslan[3], Volkan Tugcu[4], Suheyla Apaydin[1]
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Background: Open surgery is the gold standard method for kidney transplantation, but in recent years robot assisted surgery is preferred because it is minimally invasive and has less complication rates. Unlike the open surgery in robot assisted surgery, the kidney allograft is placed in intraperitoneal cavity. Literature review suggests that patients undergoing renal biopsy due to allograft dysfunction should have laparoscopic biopsy with general anesthesia due to technical difficulties and hemorrhage risk.
Methods/Materials: An ultrasound-guided renal biopsy was performed by interventional radiology at our clinic, to the patients who had robot assisted kidney transplantation and had allograft dysfunction. Kidney transplant patients who underwent open surgery or robot assisted surgery were compared in terms of size of biopsies, the number of glomeruli and post-biopsy complications. Statistical analyzes were performed on the SPSS Statistics 22.0 program.
Results: Of the patients who underwent renal biopsies seven patients had robot assisted surgery and 32 patients had open surgery. There was no significant difference between age, gender or having cadaveric or living donors between the two groups. Also there was no difference between the number of glomeruli of the biopsies. Complications such as hemoglobin decline, hematoma, hematuria and pain after the biopsy were not different between the groups. No arteriovenous fistula formation, perirenal infection, organ injury or loss occurred in any of the patients.
Conclusion: Laparoscopic renal biopsy recommended for allograft dysfunction in patients with robotic kidney transplantation may be problematic for the need of general anesthesia and for patient comfort. In our study, we showed that an ultrasound-guided percutaneous renal biopsy approach is diagnostic and safe like the open surgery method in robot assisted kidney transplant patients.

	Robotic Assisted Surgery (n = 7)	Open Surgery (n = 32)	p
Age	35 ± 6	41 ± 13	0.07
Gender (Male / Female)	4 / 3	23 / 9	0.4
Cadaveric / Living donors	1 / 6	8 / 24	0.5
Biopsy size	3.8 ± 0.5	2.7 ± 0.9	0.01
The number of glomeruli	25 ± 10	22 ± 11	0.5
Hemorrhage (hemoglobin decline)	1	3	0.7
Hematoma	0	1	0.6
Hematuria	0	5	0.3
Pain	1	5	0.9
Arteriovenous fistula	0	0	–
Perirenal infection	0	0	–
Organ injury or loss	0	0	–

Basic Lung Surgical Technique

BOS557 INDICATIONS FOR PROPER USE OF INTRAOPERATIVE EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN LUNG TRANSPLANTATION: OUR RECENT EXPERIENCE

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Background: The role of "Extracorporeal Membrane Oxygenation" (ECMO) in lung transplantation (LTx) is debated because of the absence of shared guidelines. It is unclear whether ECMO should only be used as intraoperative assistance for the purpose of cardiorespiratory support in selected cases or if it should be considered as a preventive standardized support strategy. Our study aims to compare the outcome of transplanted patients with and without ECMO, taking into account all peri-operative variables.
Methods: We considered all transplants between January 2012 and December 2015, with a retrospective analysis. A total of 50 procedures were performed in this period and they were divided into 2 groups: (A) with ECMO;

(B) without ECMO. In group A we included patients who underwent circulatory assistance before transplantation, and patients with indication to ECMO at the beginning of the procedure.
Results: Among the 50 patients, 23 (46%, group A) required ECMO, 27 (54%, group B) did not. The most common indication for LTx was Cystic Fibrosis in group A (CF = 10; IPF = 7; COPD = 3; Other = 3) and Pulmonary Fibrosis in group B (IPF = 15; COPD = 5; CF = 5; Other = 2). No differences were revealed between the 2 groups regarding ICU stay, hospitalization, postoperative morbidity and mortality. Overall survival was 100% (A) and 87% (B) at 1 month; 91% (A) and 86% (B) at 1 year. Our study provides evidence of an important risk factors before LTx: number of days on the waiting list before the operation, with a medium of 423 days (A) and 330 (B). Intraoperative differences were hemorrhagic complications and blood transfusions, with increased risk in heparinized patients undergoing ECMO.
Conclusions: There were no large differences in morbidity and mortality, between the 2 groups. ECMO has proven itself useful in patients with high risk factors, as a period >1 year on the waiting list, pulmonary hypertension and Cystic Fibrosis, to prevent intraoperative cardiorespiratory failure.

Basic Lung Other

BOS558 MESENCHYMAL STEM CELL TREATMENT IN A TRANSLATIONAL EX VIVO LUNG PERFUSION SYSTEM

Maximilia Hottenrott[1], Mojtaba Parvizi[2], Judith Van Zanden[3], Susanne Veldhuis[4], Petra Ottens[4], Henri Leuvenink[4], Marco Harmsen[2], Michiel Erasmus[3]
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Ex vivo lung perfusion (EVLP) increased the donor pool in some centers by 20%. However, this treatment has been limited to lungs with edema. While a great majority of lungs is being rejected for transplantation as a result of inflammation. Mesenchymal stem cells (MSCs) have been identified as multipotent treatment for proinflammatory diseases. The aim of this study was to identify their effect in a translational rat EVLP model. Therefore, heart-lung blocks were procured from Lewis rats 3 h after explosive brain death induction and were cold preserved for 1 h in Perfadex at 4°C. Thereafter, lungs were placed for 6 h in a normothermic EVLP model. Lungs were ventilated with a tidal volume of 7 ml/kg of body weight, a PEEP of 5 cm H_2O, a frequency of 60 and a FiO2 of 21%. Perfusion was performed with a modified Steen solution and cefuroxime at a mean pulmonary aterial pressure of 12 mmHg, with and without administration of 1×10^6 MSCs 5 min after reperfusion intra-arterially. Ventilation parameters, lung oxygenation capacity, glucose levels, lactate and flow were noted, over time. Lungs were analyzed for wet/dry ratio and qPCR. MSC treatment led to a significantly reduced pulmonary inspiratory pressure at the end of EVLP. Unexpectedly, flow and wet/dry ratio did not differ between groups. To maintain glucose levels stable more glucose had to be added in the presence of MSCs, respectively. There was no difference in lung oxygenation capacity, proinflammatory gene expression or lactate production. MSC were located in the capillaries after EVLP. In conclusion, MSCs have no immediate antiinflammatory effect and little effect on fluid clearance, but fortunately seem to have no adverse effect. However, metabolic changes need to be analyzed further and whether this might be the result of microcirculatory changes.

Clinical Lung Rejection

BOS559 AWAKE EXTRACORPOREAL MEMBRANE OXYGENATION BRIDGING FOR PULMONARY RETRANSPLANTATION: CASE REPORT

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Marmara University, Turkey

Introduction: Lung retransplantation (re-Tx) is the only therapeutic option for acute and chronic graft failure. However, experience of extracorporeal membrane oxygenation (ECMO) in the setting of re-Tx is very limited. Herein we describe a Tx case supported by VA-ECMO.
Case: A 29-year-old woman affected by bronchiectasis underwent bilateral lung transplantation. Her postoperative course was complicated with cardiac

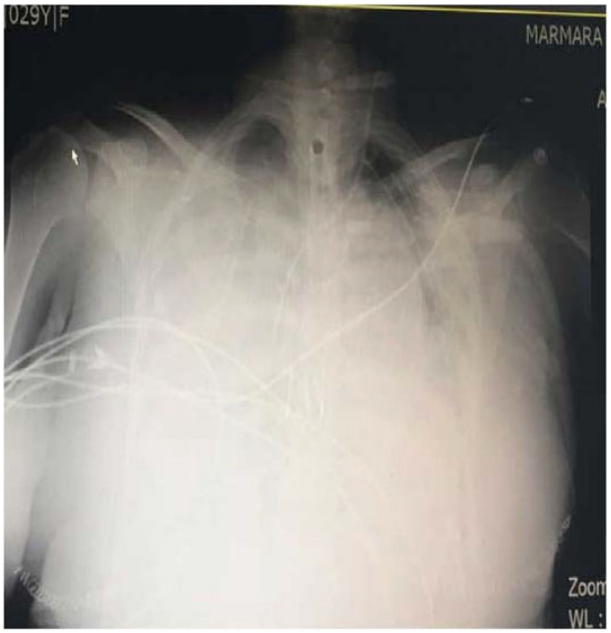

Figure 1: Chest x-ray of the patient at the time of primary graft failure.

arrest and a central veno-arterial (VA) ECMO was instituted in an urgent setting. Septic shock developed from Gram-negative bacteremia (Acinetobacter baumannii) on the 2nd day of Tx. On 3rd day, peripheral VA-ECMO was applied and sternum was closed. The empiric antibiotic was started and later colistin treatment were initiated. The patient's condition improved progressively over the next few days and surgical tracheostomy was applied. Despite aggressive therapy and awake ECMO support, the patient's pulmonary function was so poor and weaning from ECMO could not be achieved. Chest x-ray (Fig. 1) showed revealed bilateral consolidation and bronchoscopy showed near total occlusion of the right bronchial anastomosis and minimal dehiscence of the left bronchial anastomosis. Primary graft failure was diagnosed. Lung retransplantation was decided on the 30th day of Tx due to her reasonably good general and cardiac conditions associated with a young age and absence of any other organ insufficiency.
Conclusion: The treatment strategy for PGD is to gain time to improve PGD-related lung damage and to perform supportive treatments for retransplantation. In our case, after massive blood transfusions caused PDG probably and additional A. baumannii infection resulted with acute early graft failure. Post transplantation mediastinitis known as highly mortal and successfully treated in this case.

Nutritional support, management of immunosuppressive therapy, psychotherapy, active physiotherapy and VA-ECMO for the bridge treatment of retransplantation are in progress during this time. VA-ECMO for the bridge treatment of retransplantation are in progress during this time.

Clinical Lung Other

BOS560 CHRONIC PAIN 1–5 YEARS AFTER LUNG TRANSPLANTATION – A MULTICENTER STUDY

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Background: Pain has wide-reaching detrimental effects across various life-domains and also affects health related quality of life after solid organ transplantation. The extent to which lung recipients experience chronic bodily pain in the years after lung transplantation has received little attention in the literature. Therefore the aim of this study was to provide a multidimensional assessment of self-reported pain 1–5 years after lung transplantation and its relationship to self-reported psychological general well-being and self-efficacy.
Methods: This multicentre, cross-sectional study is a part of the Swedish national study: Self-management after thoracic transplantation (SMATT). In a total 117 Caucasian lung transplant recipients that were due for their yearly follow-up 1 (n = 35), 2 (n = 28), 3 (n = 23), 4 (n = 20) or 5 years (n = 11) after lung transplantation were included and 113 reported their pain. We used the Pain-O-Meter (POM), which provides information about pain intensity, quality, location and duration. In addition they responded to Psychological General

Well-being (PGWB) and the instrument Self-Efficacy for managing chronic disease.
Results: The prevalence of pain was 51% after 1 year, 68% after 2 years, 69.5% after 3 years, 75% after 4 years and 54.5% after 5 years. The three most common pain locations were the chest, the back or the legs. There were significant differences between male and female lung recipients regarding pain intensity where women experienced a higher pain intensity ($p = 0.010$) and worse sensory and affective burden ($p = 0.006$). The better perceived psychological wellbeing the lower odds for pain and the higher self-efficacy the lower probability of experiencing pain.
Conclusion: Chronic bodily pain is a common and serious symptom up to five years after lung transplantation. Female lung recipients experience more pain and pain related illness than men.

BOS561 RECOVERY AND PSYCHOLOGICAL WELL-BEING ONE TO FIVE YEARS AFTER LUNG TRANSPLANTATION – A MULTICENTRE STUDY

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Introduction: Few lung transplant recipients become fully recovered in terms of being free of symptoms or side-effects. Therefore, the question is raised if it is possible to experience good health by means of psychological general well-being despite limited recovery? The aim of this study was to investigate lung transplant recipients' recovery process and its relation to psychological general well-being and experienced health 1–5 years after lung transplantation.
Methods: This multicentre, cross-sectional, cohort study is a part of the Swedish national study: Self-management after Thoracic Transplantation (SMATT). In a total 117 lung transplant recipients that were due for their yearly follow-up one ($n = 35$), two ($n = 28$), three ($n = 23$), four ($n = 20$) or five years ($n = 11$) were included. We used the instrument Post-operative Recovery Profile (PRP) to measure the degree of recovery and The Psychological General Well-Being (PGWB) instrument to measure the psychological well-being and health. PGWB total sum-score is 132 where higher scores indicates better health status. PRP reveals five levels of recovery from not at all recovered, to fully recovered.
Findings: The response rate on the PRP was 74% ($n = 87$), where only 5.7% ($n = 5$) were fully recovered and 17.2% ($n = 15$) were almost fully recovered 1–5 years after transplantation. The dimension of partly recovered and slightly recovered constituted 46% ($n = 40$) and 3.4% ($n = 3$) respectively. In total 27.6% ($n = 24$) was not recovered at all. There was a strong and significant correlation (rs-0.720) between recovery and psychological well-being after 1–5 years. Lung recipients, that were slightly recovered or not recovered at all, reported a decreased psychological well-being.
Conclusion: It is possible to experience psychological well-being and health despite not being fully recovered after lung transplantation. During the long-term follow-up, more focus should lie on health-management and less on the degree of recovery.

BOS562 SYMPTOM PREVALENCE AND SYMPTOM DISTRESS ONE TO FIVE YEARS AFTER LUNG TRANSPLANTATION – A MULTICENTRE STUDY

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Introduction: Symptom experience is a critical post-transplant outcome, possibly affecting self-management. The aim of this study was to explore symptom prevalence and symptom distress 1–5 years after lung transplantation.
Methods: This multicentre, cross-sectional, cohort study is a part of the Swedish national study: Self-management After Thoracic Transplantation (SMATT). In a total 117 lung transplant recipients that were due for their yearly follow-up one ($n = 35$), two ($n = 28$), three ($n = 23$), four ($n = 20$) or five years ($n = 11$) after lung transplantation were included. We used the Organ Transplant Symptom and Wellbeing Instrument (OTSWI) covering eight factors with a summery score of 0–80 where lower scores indicates higher well-being. In addition, symptom distress was measured by degree of discomfort from twenty transplant specific symptoms.
Findings: The most prevalent symptoms 1–5 years after lung transplantation were tremor 66% ($n = 75$) breathlessness 62% ($n = 69$), decreased libido 60% ($n = 67$), headache 59% ($n = 67$) and need to rest due to breathlessness 49% ($n = 55$). The symptoms that were experienced as most distressing were embarrassed by one's looks, decreased libido, decreased appetite for food, need to rest due to breathlessness and headache. The overall well-being was considered good 1–5 years after lung transplantation, where the lowest well-being was reported four years afterwards.
Conclusion: This comprehensive evaluation of symptom occurrence and symptom distress reveals that the illness burden is extensive up to five years after lung transplantation without seriously limiting well-being. Furthermore, the study revealed that the most frequent symptoms were not the most distressing ones. There is a need for a systematic follow-up of symptoms at the outpatient clinic. Symptom distress might be a marker of impaired health suggesting increased need of self-management support.

BOS563 INFECTIONS AS CAUSE OF ICU READMISSION AFTER LUNG TRANSPLANTATION

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Background: Hospital and specially ICU readmissions after lung transplantation negatively affects quality of life, and costs. Reports on ICU readmission have been limited to case reports.
Methods: Prospective, 5-center study enrolling 174 consecutive lung transplant adults requiring ICU re-admission in Spain (August 2012–16).
Results: Overall, 78 (44.8%) ICU re-admissions were due to infections, with high median [IQR] APACHE II and SOFA scores: 19[15–25] and 5[3–8], respectively. Main lung diseases before transplantation were pulmonary fibrosis (38.7%) and COPD (34.7%), with 53.2% having bilateral transplants. When admitted by infection, 90-day mortality was 52.6% (compared with 25% when admitted by other causes ($p < 0.05$). Time from transplantation to ICU admission was <1 month: 35 (20.1%), 2–6 months: 50 (28.7%), 7–12 months: 20 (11.5%), and >12 months: 69 (39.7%). Main Infection site was pneumonia: 57 (73%), followed by intra-abdominal: 6 (8%) and urinary: 5 (6%). was identified in 18 (31.5%) pneumonias (2/3 being MDR), followed by Gram-positive cocci: 5 (9%) and 4 (7%). was also the top pathogen in non-respiratory infections: 8 (32.7%), 6 being MDR.
Conclusion: Pneumonia was the main cause of ICU re-admission in lung transplant, particularly within one year, whereas infections by MDR *P. aeruginosa* were the main challenge.
Supported in part by FISS PI1401296 and CIBERES.

Basic Lung Donation and Donor Types

BOS565 EFFECTS OF 17BETA-ESTRADIOL ON A SUDDEN ONSET BRAIN DEATH MODEL IN MALE RATS

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Background: Brain dead donors are the main source of organs transplanted in the world, but few treatments focusing on the microcirculatory disarrangement of brain death (BD) are available. This study aimed to investigate the effects of 17β-estradiol, as a microcirculatory modulator, in a sudden onset BD model.
Methods: Male Wistar rats were divided in 3 groups ($n = 11$/group): trepanned only (SH); submitted to BD (BD); treated with 17β-estradiol (E2, 280 μg/kg, iv) 60 min after BD (BD-E2). Anesthetized rats underwent sudden onset BD by inflating a balloon catheter in the intracranial space. After 180 min, the following experiments were performed: (a) evaluation of mesenteric microvascular perfusion by intravital microscopy; (b) expression of endothelial nitric oxide synthase (eNOS), endothelin-1, intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1 by immunohistochemistry; and (c) lung histological analysis.
Results: Proportion of perfused small vessels (<30 μm diameter) was reduced in BD rats ($40 \pm 6\%$) compared to SH ($75 \pm 8\%$, $p = 0.009$), and to BD-E2 ($67 \pm 5\%$, $p = 0.040$). Expression of eNOS increased in BD-E2 rats compared to BD ($p < 0.0001$) without differences in endothelin-1 expression ($p = 0.1766$). Levels of ICAM-1 increased in BD rats ($p < 0.0001$) and VCAM-1 was reduced in BD-E2 rats ($p = 0.0008$). Lung edema was increased in BD rats (66 ± 3 units/mm) compared to SH (46 ± 2 units/mm, $p < 0.0001$), and to BD-E2 (43 ± 2 units/mm, $p < 0.0001$). Similar results were observed regarding hemorrhage evaluation (BD: 43 ± 4 SH: 29 ± 4 units/mm, $p < 0.0077$; and BD-E2: 21 ± 2 units/mm, $p < 0.0001$).

Conclusion: Data presented showed that BD triggers mesenteric hypoperfusion, endothelial activation, and lung injury. 17β-estradiol treatment was effective in restoring perfusion and reducing lung damage. Estradiol, as a microcirculatory modulator, is a promise therapy to improve organs viability to transplant.

Financial Support: FAPESP grant 2016/13632-3.

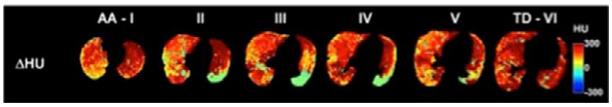

Figure 1: Maps of ΔHU recorded in a representative patient, from aortic arch (AA, I) to top diaphragm (TP, VI).

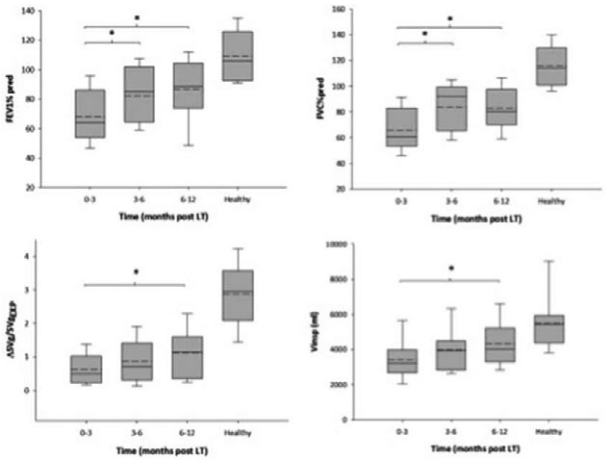

Figure 2: Changes in pulmonary function test results (FEV1% pred and FVC% pred, top panels) and quantitative CT parameters (DSVg/ SVgEXP and Vinsp, bottom panels) in 1-year follow-up. *p < 0.05.

Clinical Lung Ischemia-Reperfusion and Preservation

BOS566 PRESERVATION SOLUTION AFFECTS THE IMMUNOLOGICAL MILIEU IN LUNG TRANSPLANTATION AND ALTERS THE INFLAMMATORY BALANCE

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Background: The pro-/ anti-inflammatory balance in lung transplantation is shaped by the pulmonary immune compartments, i.e. the T and NK cell repertoire. At present, it is unknown whether the perfusion solution may influence the microenvironment of the lung. Therefore, perfusion solutions Perfadex® (PER) and Celsior® (CEL) after transplantation and peripheral blood of lung transplant recipients were analysed for their lymphocyte composition and the cytokine, chemokine, growth factor profile.
Methods: Lymphocytes from peripheral blood and perfusates of 42 lung transplant recipients (PER $n = 19$ and CEL $n = 23$), were isolated and T and NK cell subsets were analyzed by FACS; 70 cytokines, chemokines were quantified by protein multiplex analyses.
Results: Compared to the peripheral blood repertoire, lung-derived lymphocytes obtained from perfusates displayed increased frequencies of NK cells, CD69+ CD8+ and CD4+ T cells and KIR2DL1+, KIR2DL3+, KIR3DL1+ T and NK cells. In CEL perfusates, increased numbers of CD8+ T cells ($p = 0.023$) and reduced CD4+ T cell numbers with an altered CD4/CD8 ratio ($p = 0.045$) were observed compared to PER perfusates which correlated with increased CD8+ T cells, KIR2DL2+ KIR3DL1+ T cells in blood postoperatively in CEL recipients vs. PER recipients ($p = 0.0071$). Moreover, higher CD69+ T and NK cells were detected in perfusates ($p < 0.01$) indicating that they were originating from lung tissue. Regarding the protein microenvironment, IL-6, Ang-2 and VEGF-C levels were elevated in PER vs. CEL perfusates ($p < 0.05$) which correlated postoperatively with significantly higher IL-6 levels in PER compared to CEL recipients ($p = 0.003$).
Conclusion: Here, we unravel a novel mechanism of immune alterations subsequent to the application of perfusion solutions by changing composition of pulmonary T and NK cell subsets. In summary, lymphocyte subsets and cytokine release may be influenced by the perfusion solutions and potentially affect the pro-/ anti-inflammatory balance.

Translational Lung Other

BOS567 QUANTITATIVE COMPUTED TOMOGRAPHY ANALYSIS OF PULMONARY EVOLUTION DURING FIRST YEAR AFTER LUNG TRANSPLANTATION

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Background: Functional analysis of computed tomography (CT) imaging in lung-transplanted patients is an emerging tool for the interpretation of parenchymal evolution after lung transplantation (LT). Aim of this study was to determine the trends of pulmonary function indices and quantitative CT parameters within 1-year follow-up.
Methods/Materials: We prospectively collected pulmonary function tests (FEV1, FVC) and inspiration/expiration CT scans of LT patients at standard time-points (3–6–12 months). Specific gas volume (SVg, ml/g) was measured on CT images as previously described (Salito et al, Radiology 2009; Aliverti et al, ERJ 2013). Selected quantitative indexes were lung volume at inspiration (Vinsp) and the difference between inspiration and expiration SVg normalized on expiration SVg: ΔSVg/SVgEXP. Patients who experienced uneventful 12 months postoperative course after bilateral LT were included.
Results: Fifteen patients completed the trial. The Fig. 1 shows ΔHU maps recorded in a representative patient. As expected, FEV1 and FVC values significantly improved at each time-point until the 12-month check (Fig. 2, top panels). Correspondingly, Vinsp and ΔSVg/ SVgEXP increased in the same fashion with a trend toward healthy values (Fig. 2, bottom panels).
Conclusion: This preliminary trial evidenced the reliability of specific gas volume analysis as an attractive quantitative CT parameter of lung function after LT. Future studies are requested to verify the accuracy of specific gas volume analysis in the evaluation of patients with lung allograft dysfunction.

Clinical Lung Infection

BOS568 ASSESSMENT OF CYTOMEGALOVIRUS (CMV) SPECIFIC AND OVERALL IMMUNE RESPONSE IN LUNG TRANSPLANT PATIENTS WITH POSITIVE CMV SEROLOGY PRE-TRANSPLANTATION

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Background: CMV seropositive patients are considered in risk to develop CMV infection in lung transplant recipients (LuTR). The aim of this study is to identify patients who may or may not develop CMV infection by measuring CMV-specific immune response (Quantiferon®) in combination with overall immune response (Immuknow®) in a group of CMV seropositive LuTRs.
Methods: A prospective, observational, multicentre study including 92 patients at 3 months post-transplant. Both test (Quantiferon® and Immuknow®) were performed at 3, 6, 8, 10 and 12 months post-transplant. CMV prophylaxis length indication was 6 months. Cut off for Quantiferon® was 0.2 UI of interferon gamma/mL and >225 ng of ATP/mL for immuknow®.
Results: Twenty patients (21.7 %) developed significant CMV infection (DNAemia >1000 copies/mL) and 4.3% ($n = 4$) suffered CMV disease. Twenty-six (28.2 %) patients registered adverse reactions related with prophylaxis, in 9 (34%) withdrawal of prophylaxis was required.

From withdrawal of prophylaxis up to 12 months, 14 of 69 (20.3 %) patients with Quantiferon® > 0.2 UI / ml developed significant CMV infection and one of 14 (7.1%) with Immuknow® >225 ng of ATP/mL. However none of 13 patients with Quantiferon® > 0.2 UI plus Immuknow® >225 ng developed significant CMV infection.

Quantiferon® > 0.2 UI/ml plus Immuknow® >225 ng/ ml showed 19.1% of specificity and 100 % of sensitivity. Positive and negative predictive values were 22.5% and 100% respectively.

Conclusions: Quantiferon® and Immuknow® test in combination may be useful to identify patients who will not develop significant CMV infection in lung transplant patients with positive cmv serology pre-transplantation.

Translational Lung Immunology

BOS569 IMMUNE MONITORING-GUIDED TREATMENT OF A PEDIATRIC PATIENT WITH SEQUENTIAL GVHD, ACUTE REJECTION AND CMV INFECTION FOLLOWING LUNG TRANSPLANTATION

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Background: A 17 year old patient with cystic fibrosis (HLA-A11+, CMV-) underwent bilateral lung transplantation (donor: HLA-A32+, CMV+). Immunosuppression (IS) consisted of Tacrolimus, MMF and Prednisone. After an uneventful course of 3 months, he developed histology-proven cutaneous GvHD that was treated successfully by withdrawal of MMF. Then, he developed acute rejection treated by a steroid pulse. While lung function returned to normal, a CMV infection emerged despite valganciclovir prophylaxis.

Methods: Frequencies of HLA-A32+ donor lymphocytes were measured by FACS. ELISpots were performed to detect allospecific (rejection vs. GVHD) and CMV-specific T cells. HLA-A2/NLV-pentamer staining was used for frequencies of CMV-specific CD8+ CTL. Plasma cytokines were measured by multiplex assays.

Results: With development of skin GvHD, frequencies of 3–4% HLA-A32+ donor CD4+, CD8+ T cells, 5–8% B and 1–4% NK cells were detected. Donor T, NK cells declined after MMF withdrawal, but B cell frequencies remained stable. Parallel to improvement of GVHD, acute rejection developed, accompanied by significantly increased allo-A32-specific CD8+ T cells within one week, which declined upon steroid pulse. Allo-HLA-A11-restricted T cells, responsible for GvHD, were found at low frequencies. Steroid pulse was accompanied by serological detection of CMV which induced HLA-A2/NLV specific CD8+ T cells producing IFN-g in response to CMV peptides. CMV viremia disappeared with emergence of CMV-specific CTL. Plasma levels of sCD25, IFN-g, IL-17 responded to IS alterations, to pulsed steroids with a transient drop.

Conclusions: Using specific immune monitoring tools, we could confirm clinical diagnoses of the patient. Frequencies of allo- or virus specific T cells, donor lymphocytes and plasma cytokine levels followed the clinical course of GVHD, followed by rejection followed by CMV infection. The modification of IS by using immune monitoring information resulted in stable recovery for months.

Clinical Lung Other

BOS570 SAFEGUARDS AND PITFALLS OF EXTRACORPOREAL MEMBRANE OXYGENATION AS BRIDGE TO LUNG TRANSPLANTATION

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Hospital Universitario Fundación Favaloro, Argentina

Introduction: Extracorporeal membrane oxygenation (ECMO) has been proposed as an alternative bridging mode to mechanical ventilation and this is an evolving management technique of rapidly progressive pulmonary disease. The aim of this study was to assess the current evidence regarding how the ECMO strategies have changed over the last years.

Methods: Retrospective review. Single-institution's experience. From 2010 to 2016, we performed 97 ECMO Runnings in 90 p, of these, 35 p were bridge to lung transplant (BTT). We divided this cohort in two groups by era (Group 1: 2010-2012 and Group 2: 2013-2016). Categorical data were shown as frequencies/percentages and continuous data as means with standard deviation. Fisher's exact test and the chi-square analysis were performed to compare continuous and categorical variables, respectively. Actuarial survival was estimated with the Kaplan–Meier method.

Results: Eight p were BTT in group 1 and 27 p in group 2. Overall median recipient age was 34.7 ± 19.4 years. The etiologies were: cystic fibrosis (CF) ($n = 15$), idiopathic pulmonary fibrosis ($n = 7$), secondary pulmonary fibrosis ($n = 4$), pulmonary arterial hypertension group 1 ($n = 3$), pulmonary hypertension group 3 ($n = 4$) and 3 p with non CF bronchiectasis. Veno-venous ECMO mode was used in 17 p (48.5%), veno-arterial in 11 p (31.4%), arterio-venous in 3 p (8.5%) and veno-arterio-venous in 4 p (11.4%). Fourteen p underwent sedated bridging, 14 p awake and 7 p ambulatory ECMO strategy. Overall successful bridging was 59 % (20% vs 75% group 1 and 2 respectively, $p < 0.05$). All p survive lung transplant except one. Survival rate at 1 year was 75%.

Conclusions: Training program for patients on ECMO as BTT is an important goal because it improves overall patient conditioning for lung transplantation. In carefully selected patients, ECMO is a safe and effective mean of bridging decompensated patients with end-stage lung disease to lung transplantation.

Clinical Pediatric Transplantation Other

BOS570.1 PAEDIATRIC RENAL TRANSPLANT SURGICAL SAFETY CHECKLIST – VALIDATION USING A NOVEL INDIRECT METHOD

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Background: Complexity in paediatric renal transplantation is caused by immunological, technical and size mismatch considerations, in addition to differences in perioperative care compared to adult practice. Paediatric renal transplant surgical checklists (PRTSC) have not been developed and validation remains cumbersome due to the multidisciplinary nature of the process. This study aims to validate such a checklist using a novel method of thematic coding based on previously validated checklists from related surgical specialties.

Methods: A PRTSC was developed by a panel of transplant experts using a group consensus method. Previously validated checklists were analysed, segregated and coded into individual safety items (checks). The validated thematic codes were mapped to determine overlap with PRTSC safety items in order to ascertain validity.

Results: Four established and previously validated checklists were used as gold-standards. These consisted of the generic World Health Organization (WHO) checklist, adult and paediatric general surgical checklists, as well as an adult transplant checklist. Sixty safety checks were identified in total (48 general, 80%; 12 transplant-specific, 20%). Overall concordance between PRTSC and grouped validated data was 88%. Specifically, there was a concordance of 96% with the WHO generic checklist, 88% with the general paediatric checklists and 96% with the adult transplant checklist. No items were present in the PRTSC that had not been previously validated in other checklists.

Conclusions: The development of unit and specialty-specific checklists is recommended by the WHO, but validation is essential for safe clinical practice. The new validation method described suggests that the new paediatric renal transplant surgical checklist shows good congruity with previously validated checklists and may therefore be valid. This may represent a novel method of clinically validating new checklists based on existing expertise.

Clinical Pediatric Transplantation Infection

BOS570.2 MULTI-DRUG RESISTANT CMV VIREMIA SECONDARY TO A RARE VIRAL MUTATION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENT SUCCESSFULLY TREATED WITH ANTI-PROLIFERATIVE CESSATION AND IMMUNOGLOBULINS ONLY

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Introduction: International Transplant Society for CMV Consensus Group advises ganciclovir, valganciclovir and foscarnet as treatment for CMV in transplant recipients. Viral DNA polymerase resistance mutations are rare but may be associated with cross resistance. We report a rare CMV mutation associated with resistance to all available medications in a CMV seronegative recipient treated with immunosuppression dose reduction and IVIG.

Methods: Retrospective data analysis from medical records.

Results: Sixteen year old girl with end stage renal disease due to Alport Syndrome received deceased donor kidney transplant (HLA mismatch 120; CMV Donor +/Recipient -; EBV Donor -/Recipient +). Basiliximab was used for induction and tacrolimus, azathioprine and prednisolone for maintenance immunosuppression. Two months post-transplant, whilst on valganciclovir prophylaxis as per our centre's protocol, she developed CMV viremia. Viral loads continued to rise (highest log 5.41) despite the treatment dose intravenous ganciclovir. She was found to have a rare CMV UL 54 mutation (POL gene deletion 981/982) associated with multidrug resistance. She had no evidence of CMV disease and stable graft function, and was managed with cessation of azathioprine and intravenous immunoglobulins (IVIG). She remained well and had cleared viremia after six months. CMV IgM was positive at 4 months, with IgG seroconversion demonstrated at 9 months post-transplant. She had borderline T cell mediated rejection successfully treated with high dose of oral prednisolone. Eighteen months post-transplant, patient is well with stable graft function (estimated GFR 69 ml/min/1.73 m^2) on tacrolimus and daily prednisolone. To date, cytotoxic T cell response to CMV is negative but CMV remains undetectable.
Conclusion: We report a case of multidrug resistant CMV viremia in a patient with primary infection, managed with IVIG and cessation of anti-proliferative agent with excellent patient outcome and good graft function.

Clinical Pediatric Transplantation Other

BOS571 A SINGLE CENTER EXPERIENCE OF LIVER-KIDNEY TRANSPLANTATION IN CHILDREN

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Background: Pediatric liver-kidney transplant (LKT) is performed in autosomal recessive polycystic kidney disease (ARPKD), primary hyperoxaluria type 1 (PH1) and in less frequent in born metabolic diseases. We report our experience in pediatric LKT, performed between 2010 and 2016.
Methods and results: A total of 13 patients (10 F) with median age of 8.9 years (range 1.7–18 years), on dialysis prior to transplantation, underwent LKT. Indications were ARPKD in 6 patients (46.2%) and PH1 in 7 patients (53.8%). 10 patients (4 PH1 and 6 ARPKD) received simultaneous LKT, 3 patients with PH1 underwent sequential, liver-first, transplantation. Cadaveric LKT was performed in 11 children, using 7 whole livers and 4 partial grafts; sequential living donor LKT (time interval 8 and 20 months) was performed in 2 children with PH1, one from the same donor and one from different donors. In all PH1 patients hemodialysis was performed during combined LKT to reduce the risk of oxalate deposition in the renal graft. 3 patients had postoperative complications: hemorrhage ($n = 2$) and biliary stenosis ($n = 1$). 3 patients (23%) had biopsy-proven acute cellular rejection requiring steroids pulse: one renal ACR, 6 months after LKT, and 2 liver ACRs, 3 and 12 months after LKT, respectively. 12 children (92.3%) are alive with good liver and kidney function after a median follow up of 4.5 years (range 0.3–6.5). One patient with PH1 died from hemorrhage 8 days after LKT.
Conclusion: LKT is effective in children with ARPKD and PH1. Different type of liver grafts, from cadaveric and living donor, can be used with similar good results. In PH1 patients, peritransplant hemodialysis and a proper choice between combined and sequential LKT is critical to avoid early kidney graft damage.

Clinical Pediatric Transplantation Cancer

BOS572 GRAFT FUNCTION AND REJECTION AFTER POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD) IN PEDIATRIC KIDNEY RECIPIENTS UNDER MTOR-INHIBITOR BASED IMMUNOSUPPRESSION

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Data on graft function in pediatric kidney recipients after posttransplant lymphoproliferative disease are scarce.

We investigated estimated glomerular filtration rate (eGFR) of children after kidney transplantation (KTx) at and yearly up to 3 years after diagnosis of PTLD.

The 9 children (3 girls and 6 boys) had a mean age at KTx of 6.8 ± 4.8 years. 7 children were treated with 6 courses of rituximab according to the PED-PTLD-2005-protocol; one child additionally received mCOMP therapy. In two children, immunosuppressive therapy was reduced only; in one patient calcineurin inhibitor (CNI) was reduced and in a second patient azathioprine was switched to low dose-CNI. In 7/9 children, immunosuppression was switched to an mTOR-inhibitor-based regimen. Rang based ANOVA showed no decrease in eGFR 1, 2 or 3 years after diagnosis of PTLD ($p = 0.9779$). 4 patients developed donor-specific antibodies during observation time (in the same year as diagnosis of PTLD, after 3 years, after 5 years, after 6 years). Only one patient developed chronic antibody-mediated rejection 12 years after diagnosis of PTLD and lost her graft one year later.

In conclusion, eGFR of patients with PTLD is stable in long time observation under a reduced, mainly mTOR-inhibitor-based immunosuppression without an increased rate of cAMR.

Clinical Pediatric Transplantation Other

BOS574 INNOVATIVE APPROACH TO ENGAGE AND MANAGE TEENAGE AND YOUNG ADULT TRANSPLANT RECIPIENTS: USER VIEWS OF A COMMUNITY BASED YOUNG ADULT SERVICE

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Background: The incidence of end-stage renal disease (ESRD) amongst young adults is increasing. This group of patients often report low self-worth and exhibit difficulties in education, employment, and maintaining relationships. Moreover, 35% of young adults lose a successfully functioning kidney transplant within 36 months of transitioning from paediatric to adult services. The Oxford Young Adult Clinic (OYAC) is a pioneering service designed to target poor outcomes by bringing together young adults for clinics, social events, and 1:1 support. With clinics held in universities, canal boats, and music festivals, patients rarely need to visit hospitals.
Methods: Based on previously validated questionnaires and adopting 5-point Likert scales, we generated an internal evaluation of the OYAC designed to assess the OYAC's benefits and limitations in comparison to standard hospital clinics. The questionnaire was administered and analysed by a dedicated researcher. In total, 43 patients attend the OYAC. We report preliminary findings from 21/43 (49%) of the study population although the study is ongoing.
Results: Overall, 100% of individuals reported that they preferred attending the OYAC over standard hospital clinics. The OYAC enhanced patients' independence, understanding of their medical condition and medications, and their relationships with medical staff (Figs 1 and 2).

The OYAC has a full-time youth worker (YW) to catalyse peer interaction and provide 1:1 support. 100% of individuals reported that the YW's input was important or very important, and 85% reported that the YW could help patients overcome difficulties in their lives.

Conclusion: The results indicate the success of the OYAC in delivering a service that integrates clinical care with dedicated peer and social support to address obstacles faced by young adults with ESRD. The OYAC model is a simple but a more effective care pathway for engaging young adult patients than standard clinical practice.

BOS575 SMARTY: AN E-HEALTH TOOL FOR COMMUNICATION BETWEEN PATIENTS, FAMILIES AND MEDICAL CARE TEAMS AFTER PEDIATRIC LIVER TRANSPLANTATION

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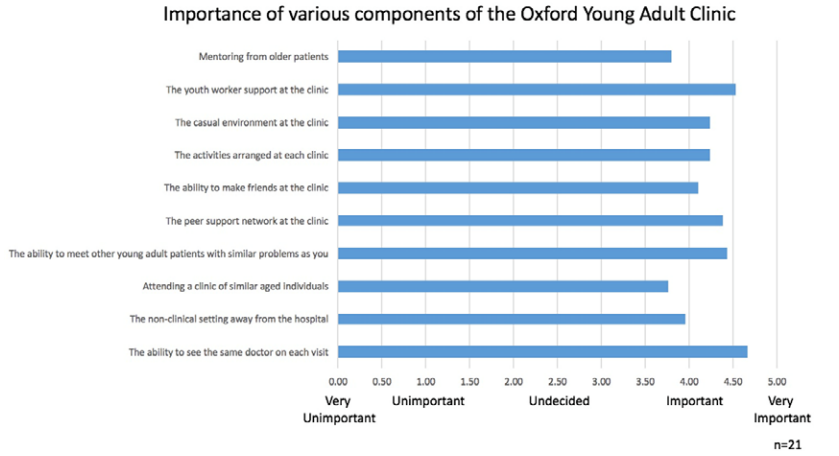
Background: Care management of children after liver transplantation is demanding. Tools for efficient communication between families, the medical team in transplant centres and primary care pediatricians do not exist or do not adhere to privacy regulations. We developed and implemented an e-health tool (SMARTY) to enable safe and efficient communication in this setting.
Methods: Families/patients signed consent forms before enrolment. Their pediatricians in primary care were asked to participate. All pediatric hepatologists at University Children's Hospital in Tübingen participated. Families with insufficient language skills were excluded. Participants downloaded the SMARTY software on a PC or smartphone and were asked to mainly communicate through the secure platform. Patients received a personal virtual



'treatment-room' in SMARTY. After exploratory interviews, questionnaires for care-givers and families were developed. Their experiences with communication and care were evaluated before introduction of SMARTY, after 1 year and will be after 2 years. Time invested in communication and number of ambulant and in-patient visits before and after SMARTY will be compared. The study was approved by local ethics and data privacy committees.
Results: of 51 invited families of transplanted children, 5 declined participation, 7 did not reply. Currently, 5 local pediatricians actively participate, 10 are interested but have not been active, 6 local care-givers declined. In total ca. 96 messages/month were exchanged concerning 51% of the 39 active families (mean 4.8/family/month), the others had < 1 contacts/month. Most messages concerned management adaptation (35%) and general questions (53%). Laboratory data were exchanged 15×/month (mean).
Conclusion: In preliminary analysis the SMARTY tool enables safe, reliable communication between families and care-givers after pediatric liver transplantation. User satisfaction and potential to decrease workload will be analysed.

Clinical Pediatric Transplantation Donation and Donor Types

BOS576 PEDIATRIC DONATION – CONSENT RATES IN DIFFERENT AGE GROUPS

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Background: Only few data are available regarding consent rates in pediatric organ donation. In Germany children from the age of 14 years can refuse, from the age of 16 years they can approve organ donation. If no will during life time has been expressed, their next relatives have to decide. This is a follow up analysis to our first study. We analyzed, whether there are differences in consent rates between different age groups.
Methods: All potential organ donors aged 18 yrs or younger reported to the German OPO from 1/2006–12/2016 were included. Different age groups were formed: group 1 (g1): <1 year (n = 75); g2: 1–5 years (n = 190); g3: 6–15 years (n = 322); g4: 16–18 years (n = 275).
Results: 862 potential donors ≤18 years (g1–4) could be analyzed. Altogether, the consent rate in pediatric donors is comparable to those in adult donors in Germany (67%; 2015). In 572 cases (66.3%) consent to organ donation was given, in 278 cases (32.2%) donation was refused, and in 13 cases (1.5%) due to medical reasons the process was stopped before family approach. The consent rate for the pediatric donors varied between the different age groups, being the lowest in donors aged 1–5 years: 56.3% (g2, n = 80), followed by 62.7% (g1, n = 47), 69.6% (g3, n = 224) and 69.8% (g4, n = 192).
Discussion: Overall, this follow up confirms the results of the first study. We experienced that parents' decision especially in the age g2 to g4 is based at least partially on the fact that they observe their children's interaction with their environment. Older children (g3–4) often show the ability to express empathy with ill and weak humans, our experience shows that this is taken into account when deciding about organ donation. This might explain the higher consent rate in g3–4. Infants (g1) are at the lowest level of social interaction, thus, parents have to decide mainly due to their own moral concepts. They report that – when giving consent to donation – their main motivation is to give sense to the senseless death.

Clinical Pediatric Transplantation Other

BOS577 KIDNEY RE-TRANSPLANTATION IN CHILDHOOD-FEASIBILITY AND OUTCOMES

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Introduction: Kidney transplantation (Tx) has been increasing in small children. This may lead to more children needing 2nd Tx during childhood. This study looked into the characteristics of renal transplant recipients who underwent more than 1 Tx during childhood.

Methods: Single centre retrospective analysis of all paediatric kidney transplants during 2003-2015.
Results: One hundred and seventy one transplants were performed, nine of which were re-transplants (5.3%). At last follow up (median 8 years; IQR 10 years), there was no difference in graft survival for children with a single Tx compared with those re-transplanted ($p = 0.255$).

Of the re-transplanted patients, eight had two and one had three transplants (80% deceased donors at 1st Tx; 50% at 2nd Tx). Recurrent acute rejections caused graft failure in four patients, 2 had chronic antibody mediated rejection, 2 thrombosis and one FSGS recurrence as cause for graft failure. All patients were CMV and EBV naive at 1st Tx. Two patients have previously undergone Tx onto aorta/IVC and had a re-transplant to the same vessels. Five were HLA sensitized, one highly (cRF>85%). The difference in graft survival at 3 year follow-up between first and second transplant was not significant (98% and 88% respectively; $p = 0.2$). Three patients lost 2nd graft before adulthood due to chronic antibody mediated rejection and BK virus allograft nephropathy, one of which received 3rd Tx at the age of 8 years.
Discussion: The re-transplantation rate is low in this cohort. Despite surgical and immunological challenges kidney re-transplantation in childhood is feasible and with good outcomes; this should be accounted for when consenting and determining the management for young recipients.

Translational Pediatric Transplantation Other

BOS578 PARENTS' EXPERIENCES OF REQUESTS FOR ORGAN AND TISSUE DONATION: EVIDENCE FROM A QUALITATIVE STUDY

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Background: A proportion of children with complex and life-threatening conditions (LTC) die, which makes them potentially eligible to be organ and/or tissue donors. While research has focused on documenting donation rates and establishing best practice, relatively little is known about parents' experiences of requests (or not) for donation. Increasing our understanding of parents' experiences will hopefully enable improved decision-making and support.
Methods: Bereaved parents and parents of a child with a LTC were interviewed to investigate their experience of requests for organ and tissue donation. Parents were recruited through 2 neonatal intensive care units (ITU), 2 Paediatric ITUs, 1 Cardiac ITU and a children's hospice. Parents were asked about donation, specifically whether they were asked, and their experiences related to the request and the donation (if applicable). A thematic analysis was carried out to generate overarching themes.
Results: 24 parents of 20 children were interviewed: 21 bereaved parents and 3 parents of a child with a LTC. 7 parents/children were asked about donation (13 not asked), 4 of those agreed and 2 actually donated. Five overarching themes were identified: 1) difficulty of timing of the request, 2) importance of altruism and the child's legacy around decision-making, 3) request, or lack of request, as a judgement/indication of the child's value, 4) emotional cost to staff and 5) negative aspects, e.g. paperwork, brain death tests.
Conclusion: The findings highlight that parents are aware of the cost to staff in having to ask, and that there is an emotional cost for parents when they are not asked, as they interpret this as a judgement about the value of their child. None of the parents reported insensitive or inappropriate approaches by health professionals. Our study suggests that a request should be made, if eligibility allows, as parents can derive comfort from the thought that their child might be suitable for donation.

Clinical Pediatric Transplantation Other

BOS579 LIVER TRANSPLANTATION IN MAPLE SYRUP URINE DISEASE (MSUD): A SINGLE CENTER EXPERIENCE

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Introduction: MSUD is an autosomal recessive metabolic disorder characterized by impaired activity of the branched-chain acid dehydrogenase complex. If left untreated, MSUD can result in mental illness and even death. Liver transplantation (LT) has been effective in patients with MSUD. Liver from patients with MSUD can be used for domino LT (DLT).
Methods and results: Between 2008 and 2016, 4 out of 168 (2.5%) children underwent LT for MSUD, with mean age of 47.5 months. A patient with MSUD who underwent LT provided a whole liver (WL) for DLT in a child with biliary cirrhosis. Indications to LT were poor metabolic control, expressed as psychomotor disabilities and poor quality of life. 3 patients received cadaveric grafts (2 left lateral segment [LLS], 1 WL) and 1 a LLS from living related liver transplant (LRLT) from the heterozygous father. After LT, all patients had noticeable decrease branched-chain amino-acids and alloisoleucine (from 133 to 9.5 μmol/l), despite the increase of the proteins in the diet to the normal requirements for age. Despite normal protein intake no post-LT metabolic decompensation were documented, including LDLR and DLT recipients. DLT recipient maintained near-normal levels of amino acids, with no detectable alloisoleucine on free diet. No surgical complication was seen after LT. One patient showed acute liver rejection, requiring steroids pulse. All the children had normal graft function after a median follow up of 6 months (range 5.25–22.5). All children had neurological improvement or stability.
Conclusion: LT in MSUD improves quality of life, reducing the risk of metabolic decompensation with a protein-unrestricted diet. Patients with MSUD can be successfully treated by LRLT, even if the donor is a heterozygous carrier, and liver from MSUD patients can be used in DLT.

Clinical Pediatric Transplantation Surgical Technique

BOS580 REPLACEMENT VS. PRESERVATION OF THE NATIVE VENA CAVA IN PEDIATRIC LIVER TRANSPLANTATION WITH LEFT LATERAL SEGMENT GRAFTS

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Background: Replacement of the native vena cava in segmental pediatric liver transplantation has been rarely described. At our centre, since 1998, the native vena cava of the children transplanted for malignant liver tumors has been replaced with a donor venous graft with the purpose of radicality.
Methods/Materials: This monocentric retrospective cohort study analyses 365 children who received a primary liver transplant with a deceased donor left lateral segment graft from November 1997 to May 2016, with a mean follow-up of 6.3 ± 4.55 years. The primary endpoint is the incidence of overall and early (within 70 days from transplantation) hepatic venous outflow complications (HVOC). The aim of the study is to verify any possible difference in the incidence of HVOC between replacement and preservation of the native vena cava.
Results: The native vena cava was preserved in 342 patients (94%, group A) and replaced in 23 (6%, group B). The two groups were homogeneous except for indication to transplantation, time on the waiting list (59 ± 72.02 days in group A, 16 ± 15 days in group B, $p = 0.005$) and graft to recipient weight ratio (3.34 ± 1.45 in group A, 2.51 ± 0.73 in group B, $p = 0.017$). Overall HVOC were 17 (5%) in group A and 2 (9%) in group B (p not significant, NS), early HVOC were 13 (4%) in group A and 1 (4%) in group B (p = NS).
Conclusion: Our experience shows no significant difference in the incidence of overall and early HVOC between replacement and preservation of the native vena cava. Caval replacement seems to be safe and effective in pediatric liver transplantation with left lateral segment grafts and may be a useful option in liver malignancies, Budd-Chiari syndrome or severe hypoplasia of the retrohepatic vena cava.

Clinical Pediatric Transplantation Infection

BOS581 COLONIZATION OF PEDIATRIC LIVER TRANSPLANT RECIPIENT WITH KPC-PRODUCING *KLEBSIELLA PNEUMONIAE*: A SINGLE CENTER EXPERIENCE WITH THE USE OF MODIFIED ANTIBIOTIC PROPHYLAXIS

Andrea Pietrobattista, Sabrina Cardile, Manila Candusso, Maria Sole Basso, Daniela Liccardo, Paola Bernaschi, Francesca Tortora, Roberto Bianchi, Marco Spada, Chiara Grimaldi, Giuliano Torre
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Background: Over the last decade, carbapenem resistant-Klebsiella pneumoniae (CR-KP) has spread worldwide becoming a serious healthcare problem. Infections with CR-KP are associated with high morbidity and mortality in liver transplantation (LT) recipients. However, there is no consensus for managing CR-KP colonized patients (pts) and particularly in the pediatrics setting.
Methods: We conducted a prospective study involving all 51 pts undergoing LT during 24-month period (January 2014–2016) to evaluate incidence and outcome of CR-KP colonization. In those identified as intestinal carrier of CR-KP, antibiotics

use was strictly limited until LT and we adopted a modified peritransplant prophylaxis. In such cases, the antibiotics were chosen based on the latest CR-KP antibiogram available, establishing a first line treatment (day 0 until day +7 post LT) and a second line to be used if CR-KP bacteremia would occur after LT.
Results: We identified CR-KP intestinal colonization in 4/51 pts (7.8%, 3 F), all with cirrhosis due to extrahepatic biliary atresia. The mean age was 9.03 months. Median PELD score was 25.2 (CR-KP negative group PELD 18.4). All 4 colonized pts were referred from abroad with an history of multiple infections; 3 out of 4 had positive CR-KP rectal swab at first sample after admission. All pts received split livers with hepaticojejunostomy with a Roux-en-Y loop for biliary reconstruction. No surgical complications neither post-LT bloodstream CR-KP infections were observed. However, detection of pathogens other than CP-KP was present in 3 pts, resulting in antibiotic treatment modification and extension. At 12 months, LT pts' survival was 100% and stool cultures were negative for CR-KP in all pts.
Conclusion: LT in children colonized by CR-KP is feasible; antibiogram-guided antibiotic prophylaxis helps to prevent morbidity and mortality. Future microbiota-targeted intervention strategies could help to avoid overtreatment and resistance development.

Clinical Pediatric Transplantation Surgical Technique

BOS582 SIMULTANEOUS PEDIATRIC LIVER AND PANCREAS TRANSPLANTATION IN A PATIENT WITH WOLCOTT-RALLISON SYNDROME

Johan Nordström, Carl Jorns, Rafal Dlugosz, Lars Wennberg, Greg Nowak
Transplantation Surgery, Sweden

Background: Children with Wolcott-Rallison syndrome is typically diagnosed with diabetes before six months of age and skeletal dysplasia within the first or second year of life. Other manifestations include repetitive episodes of acute liver failure, renal dysfunction and exocrine pancreas insufficiency. Also intellectual deficit, hypothyroidism, neutropenia and recurrent infections are associated with the syndrome.
Methods/Materials: Two previous cases of organ transplantation as treatment for Wolcott-Rallison Syndrome is found in literature, both published in recent years (2014 and 2015), both as en bloc multiorgan transplantation (liver, pancreas and kidney) in pediatric recipients. We present one case of simultaneous pediatric liver and pancreas transplantation in a pediatric recipient not using en bloc technique without kidney transplantation. Our patient had been in dialysis treatment two months before transplantation when treated in ICU for multiorgan failure that had started with an air-way infection. The decision not to transplant a kidney from the same donor was made because the renal function had recovered completely. Pediatric whole liver transplantation was performed with standard technique and immediately after arterial liver reperfusion, whole pancreas transplantation was performed using donor aorta and vena porta as vasculature for anastomoses to recipient aorta and vena cava.
Results: Liver- and pancreas function was excellent immediately. The patient was re-operated for bile-leakage from biliary anastomosis on day two postoperatively. She was also operated for nutritive jejunostomy. Six-month check-up with normal liver, pancreas and kidney.
Conclusion: The concept of treating rare, genetic disorders such as Wolcott-Rallison syndrome with organ transplantation may be an effective option in terms of managing complications and increase long-term survival.

Basic Kidney Ischemia-Reperfusion and Preservation

BOS583 TARGETING RENAL ISCHAEMIA-REPERFUSION INJURY USING HAEMOADSORPTION OF CIRCULATING INFLAMMATORY MEDIATORS IN A PORCINE EXPERIMENTAL MODEL

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University of Cambridge, United Kingdom

Background: The reduction of pro-inflammatory mediators by haemoadsorption using the Cytosorb filter may be beneficial in reducing renal ischaemia reperfusion injury.
Methods: Porcine kidneys were subjected to 22 h of cold ischaemia then reperfused ex-vivo with whole autologous blood for 6 h. Pairs of kidneys were randomised to either control ($n = 5$) or reperfusion with a Cytosorb filter ($n = 5$) in the circuit. Samples were taken for the measurement of cytokines (IL-6, TNFα, IL-8, IL-10, IL-1β, IL-1α), prostaglandin E2, C-reactive protein and measures of renal function.
Results: Levels of IL-6 and IL-8 in the perfusate and urine significantly increased during reperfusion and were significantly lower in the Cytosorb group at 6 h ($p = 0.023, 0.052$). There was a 50% reduction in the expression of IL-6 and IL-8 in the tissue at 6 h. In the control group there was a numerical increase in perfusate and urine levels of the other cytokines throughout reperfusion. Levels were consistently lower in the Cytosorb group, however this did not reach statistical significance. Levels of C-reactive protein were significantly reduced in the Cytosorb group ($p = 0.007$).

The mean renal blood flow (RBF) was significantly higher in the Cytosorb group (162 ± 53 vs. 120 ± 35 ml/min/100 g: $p = 0.022$). In the control group there was a steady decline in RBF over the first hour. In the Cytosorb group, after an initial increase in RBF, there was an abrupt fall at 30 min of reperfusion. Perfusate levels of Prostaglandin E2 (642 ± 762 vs. 3258 ± 980 pg/ml: $p = 0.001$) were significantly lower in the Cytosorb group.

Renal function was similar between groups (creatinine clearance; Cytosorb 40.5 ± 17.9 vs. control 31.7 ± 12.3 ml/min/100 g.h; $p = 0.109$).
Conclusion: Haemoadsorption can reduce the inflammatory response and improve renal blood flow during reperfusion. Nonetheless, anti-inflammatory cytokines (IL-10) and important vasodilatory mediators can also be removed by the Cytosorb filter which may be detrimental to graft function.

Translational Kidney Ischemia-Reperfusion and Preservation

BOS584 DETECTION OF INFUSED FLUORESCENT PRE-LABELED MESENCHYMAL STEM CELLS AFTER SIX HOURS NORMOTHERMIC MACHINE PERFUSION OF ISCHEMICALLY DAMAGED PORCINE KIDNEYS

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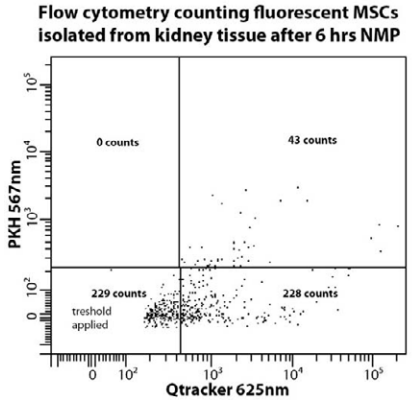
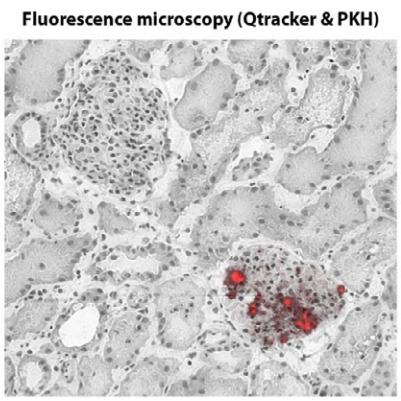
Background: Machine perfusion improves transplant outcome of marginal kidney grafts. When performed at 37°C (normothermic machine perfusion, NMP), the technique can be used as a platform for various interventions prior to





transplantation. Mesenchymal stem cells (MSCs) might modulate immune responses and diminish ischemia-reperfusion injury. Administering MSCs with NMP to transplantation could be mutually reinforcing leading to superior preservation and pre-transplant organ reconditioning. In this study, we investigated where in the kidney infused MSCs home during NMP and whether they are detectable after perfusion.
Methods/Materials: Porcine kidneys were retrieved from a slaughterhouse. After 20 min of warm ischemia and 3–4 h of oxygenated hypothermic machine perfusion, kidneys were placed on an NMP circuit and perfused for 7 h. After 1 h of NMP, either 0 ($N = 5$) or 10 ($N = 5$) pre-labeled (PKH26 and Qtracker625) human adipose tissue derived MSCs were administered. We used fluorescence microscopy and fluorescent activated cell sorting (FACS) to detect and quantify MSCs after NMP.
Results: With FACS, we detected MSCs in renal tissue after 6 h of NMP. There was a homogenous distribution of MSCs over all poles of the organ. More MSCs were detected in cortical tissue compared to medullar tissue. In venous effluent perfusate taken immediately after arterial infusion of MSCs, we could detect MSCs as well. Using fluorescence microscopy on cortical cryosection tissue we detected labeled MSCs exclusively in glomerular capillaries, but only a small portion of glomeruli were positive for infused MSCs (see Figure).

Conclusion: Pre-labeled MSCs are detectable and quantifiable in kidney tissue and perfusate after 6 h of NMP. Most cells end up in the cortex. In cortical tissue, MSCs seem to home exclusively to glomeruli. In addition, we found that not all MSCs are filtered out of the NMP circulation by the kidney in a single pass after arterial infusion.

Basic Kidney Ischemia-Reperfusion and Preservation

BOS585 RENAL IL-33 INDUCES INKT CELL/NEUTROPHIL INFILTRATION AND EXACERBATES KIDNEY ISCHEMIA-REPERFUSION-INDUCED INJURY

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Kidney ischemia-reperfusion injury (IRI) is characterized by leukocyte infiltration and renal tubular injury. Here we identify the nuclear alarmin interleukin (IL)-33 as an important and early mediator of innate immune response after kidney IR in mice. IL-33, which was found to be constitutively expressed by endothelial cells in glomerular and peritubular spaces, was immediately released from kidney tissue during IRI. Lack of IL-33 was renoprotective after kidney IRI, as evidenced in IL-33 KO mice by preservation of renal function, fewer tissue lesions, reduced neutrophil, macrophage and invariant natural killer T (iNKT) cell infiltration, and enhanced survival along with attenuated fibrosis. The reduced susceptibility of IL-33 KO mice was associated with impaired recruitment of IFN-γ/IL-17A-producing iNKT cells, known for their deleterious role in IRI as they promote neutrophil recruitment. Remarkably, iNKT cell-deficient (Jα18 KO) mice, despite their protection against IRI, showed increased levels of circulating IL-33, similarly to wild-type mice. This finding leads us to propose endogenous IL-33 as a mediator of kidney IRI as it promotes iNKT cell recruitment, activation and cytokine production, thereby leading to neutrophil infiltrates and activation at the injury site. All in all, our findings demonstrate the existence of a novel molecular mediator in the pathogenesis of renal IR and may lead to new therapeutic strategies aimed at avoiding acute kidney injury associated with renal transplantation.

BOS586 STAT1 PREVENTS RENAL FIBROSIS VIA REGULATION OF MACROPHAGE NUMBER UPON RENAL ISCHEMIC INJURY

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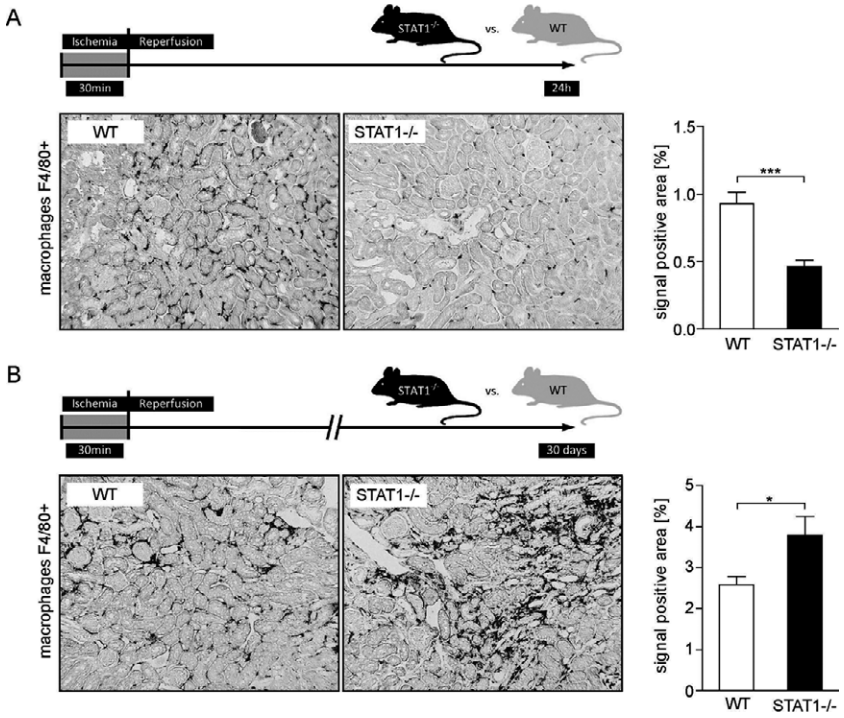
Background: Renal ischemia/reperfusion injury (IRI) leads to delayed allograft function and predisposes for interstitial fibrosis and tubular atrophy (IF/TA) in longterm follow up. The signal transducer and activator of transcription 1 (STAT1) is a regulator of the inflammatory response and tissue remodelling. Furthermore STAT1 has been postulated to be important for macrophage development. So far the role of STAT1 in renal IRI remains elusive.
Methods and results: In vitro we observed STAT1 phosphorylation and STAT1 dependent chemokine upregulation of primary murine tubular epithelial cells after 24 h hypoxia. In vivo we saw a strong upregulation of the STAT1 dependent chemokines 1, 3, 6 and 24 h after renal Ischemia (30 and 40 min respectively), but no difference in serum creatinine and urea between STAT1 knockout mice (STAT1-/-) and wild-type (WT) mice 24 h after renal IRI. Interestingly we detected immunohistochemically (F4/80+ stain) significantly less macrophage infiltration in STAT-/- mice (A). Macrophages are central regulators of the fibrogenic process, hence we studied development of fibrosis in WT and STAT1-/- mice with unilateral renal ischemia (30 min) followed by a 30 days observation time. Here we detected histologically and immunohistochemically (a-SMA stain) significantly more fibrosis in STAT1-/- mice accompanied with significantly less macrophage infiltration (compared to WT mice) (B).
Conclusions: Our observations let us assume that STAT1 could play a key role in macrophage switch and resolution of postischemic inflammation as well



as healing of IRI, orchestrating the immune response. Further investigations concerning macrophage differentiation in STAT-/- and WT mice are necessary to strengthen this hypothesis.

BOS587 NAFAMOSTAT MESILATE AMELIORATES ISCHEMIA-REPERFUSION RENAL INJURY VIA ANTI-APOPTOTIC MECHANISM

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Backgrounds: It has been reported that nafamostat mesilate inhibits inflammatory injury via inhibition of complement activation in ischemic heart, liver, and intestine. However, it is unclear if nafamostat mesilate also inhibits apoptosis in ischemia-reperfusion (IR) injured kidney. We therefore investigated whether nafamostat mesilate attenuates IR renal injury that involves inhibition of apoptosis.
Methods: HK-2 cells and male C57BL/6 mice were used for this study. C57Bl/6 mice were divided into 4 groups: sham, nafamostat mesilate (2 mg/kg) + sham, IR injury (IR injury; reperfusion 27 min after clamping of both the renal artery and vein), and nafamostat mesilate + IR injury. Kidneys were harvested 24 h after IR injury, and functional and molecular parameters were evaluated. For in vitro studies, HK-2 cells were incubated for 6 h with mineral paraffin oil to induce hypoxic injury, and then treated with various doses of nafamostat mesilate to evaluate the anti-apoptotic effects.
Results: Blood urea nitrogen, serum creatinine levels, and renal tissue injury scores in nafamostat mesilate + IR-injured mice were significantly lower than those of control IR mice (all $p < 0.01$). Nafamostat mesilate significantly improved cell survival in hypoxic HK-2 cells ($p < 0.01$), significantly decreased renal Bax expression ($p < 0.05$), and increased renal Bcl-2 protein levels in IR kidneys and hypoxic HK-2 cells compared with those of the sham and control groups. The numbers of TUNEL and 8-OHDG positive cells were significantly lower in nafamostat mesilate + IR-injured kidneys compared with those in control IR-injured mice ($p < 0.05$); nafamostat mesilate treatment decreased the expression of inducible and endothelial nitric oxide synthase in IR-injured mice ($p < 0.05$).
Conclusions: Nafamostat mesilate ameliorates IR renal injury via inhibition of apoptosis by, at least in part, lowering nitric oxide overproduction, reducing Bax, and increasing Bcl-2.

BOS588 DAPAGLIFLOZIN ATTENUATES ISCHEMIA REPERFUSION RENAL INJURY VIA HIF1 ACTIVATION

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Background: Some studies showed SGLT2 inhibition have renal protection (reduction of hyperfiltration and tubular oxidative stress) in Type 1 DM. We evaluate whether SGLT2 inhibitor, dapagliflozin reduces the renal damage via ischemia reperfusion (IR). Also, we investigate the associating molecular pathway.
Methods: In vitro, hypoxia was simulated by mineral oil in HK-2 cells. Cell survival, apoptosis signal pathway, reactive oxygen species (ROS) generation, HIF1, ERK, and AMPK were evaluated in control and hypoxic HK-2 cell with or without SGLT2 inhibitor. In vivo 10 weeks C57BL/6 mice were divided into 4 groups; vehicle ($n = 5$) and dapagliflozin (10 mg/kg) treated sham group ($n = 5$), vehicle ($n = 7$) and dapagliflozin ($n = 7$) with ischemia reperfusion renal injury. Kidneys and blood were harvested 24 h after IR injury. We performed real time RT-PCR, western blot and immunohistochemistry for molecular study and H&E stain and PAS stain for histologic examination.
Results: Dapagliflozin treatment significantly increase survival of hypoxic HK-2 cells. Dapagliflozin treatment increase the level of HIF1 in hypoxic HK-2 cells. Also it decrease the Bax/Bcl2 ratio and 8-OH deoxyguanosine generation. in vivo, Dapagliflozin treatment significantly reduced the levels of BUN and serum creatinine in IR mice ($p < 0.05$). In microscopy, dapagliflozin significantly reduced renal tubular epithelial cell necrosis and detachment in IR mice kidney. Dapagliflozin significantly increased the expression of HIF1 in IR kidney. Dapagliflozin significantly reduced the level of Bax/Bcl-2 ratio and cleaved caspase-E, 8-OH deoxyguanosine positive and TUNEL positive cells in IR kidney.
Conclusions: Dapagliflozin significantly increases HIF1 in IR injured kidney. Also it attenuates ischemia reperfusion renal injury.

BOS589 PERIOSTIN INDUCES KIDNEY FIBROSIS AFTER ACUTE KIDNEY INJURY VIA THE P38 MAPK PATHWAY

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Background: Periostin, a matricellular protein, has been reported to play a crucial role in fibrosis. Acute kidney injury (AKI) results in a high risk of progression to chronic kidney disease (CKD). We hypothesized that periostin is involved in the progression of AKI to kidney fibrosis.
Results: The patients who showed CKD progression after 3 months following AKI had a higher urine periostin/creatinine ratio than that of patients who did not. At 6 weeks after induction of unilateral ischemia-reperfusion injury, the kidneys in periostin (Postn) null mice were less atrophied, and interstitial fibrosis/tubular atrophy was significantly alleviated in Postn null mice compared with those in WT mice. The expressions of phosphorylated-p38 MAPK were also decreased in Postn null mice compared to those in WT mice. Furthermore, Postn null mice had attenuated mRNA and protein expression of fibrosis and apoptosis markers. In vitro, hypoxic injury (5% O2, 5% CO2, and 90% N2) of the human kidney-2 cells for 24 hours and 5 days increased the expressions of phosphorylated-p38 MAPK and fibrosis markers. Recombinant periostin in hypoxic conditions enhanced phosphorylated-p38 MAPK expression, which was comparable to that with recombinant transforming growth factor-β1. In contrast, inhibition of p38 MAPK ameliorated hypoxia-induced fibrosis.
Conclusion: In conclusion, periostin promotes kidney fibrosis via the p38 MAPK pathway following AKI triggered by hypoxic or ischemic insult. Periostin ablation could protect against kidney progression.

BOS591 THE MTOR SIGNAL MTOR SIGNAL REGULATES MYELOID DERIVED SUPPRESSOR CELLS DIFFERENTIATION AND IMMUNOSUPPRESSIVE FUNCTION IN ACUTE KIDNEY

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The mammalian target of rapamycin (mTOR) signal controls innate and adaptive immune response. Myeloid derived suppressor cells (MDSCs) are a heterogeneous population of myeloid cells of potent immunosuppressive capacity. In this study, we aimed to investigate the role of MDSCs in the protection of acute kidney injury (AKI) and the regulation of mTOR signal on MDSC's protective role in this context. In mice AKI model, rapamycin improved renal function, restored histological damage and decreased CD4+ and CD8+ T cell infiltration in kidney tissue. MDSCs, especially CD11b+Ly6G+Ly6Clow G-MDSCs were recruited to the injured kidney following the interaction of CXCL1, CXCL2 and their receptor CXCR2 after inhibiting mTOR signal with rapamycin treatment. The adoptive transfer of rapamycin-treated MDSCs with AKI significantly improved renal function, ameliorated histologic damages and limited T cells infiltration in kidney tissue. In addition, the expression of pro-inflammatory cytokines IL-1β and IFN-γ mRNA was down-regulated while the expression of TGF-β1 and Foxp3 mRNA was up-regulated in kidney tissue after transferring rapamycin-treated MDSCs. Adoptive transfer of rapamycin-treated MDSCs also down-regulated the serum levels of IL-1β, IL-6 and IFN-γ and up-regulated the serum levels of TGF-β1 compared with the IR group and PBS-treated MDSC group. In study, inhibiting mTOR signal regulated the induction of MDSC towards the CD11b+Ly6G+Ly6Clow G-MDSC subset. The ability to suppress T cell proliferation of both bone marrow-derived CD11b+Ly6G+Ly6Clow G-MDSCs and CD11b+Ly6G-Ly6Chigh M-MDSCs was enhanced by mTOR signal inhibition via up regulating the expression of Arginase-1 and iNOS. Taken together, our results demonstrated that MDSCs ameliorated AKI and the protective effect was enhanced by mTOR signal inhibition via promoting MDSCs recruitment, regulating the induction of MDSCs and strengthening their immunosuppressive activity.

Figure 1

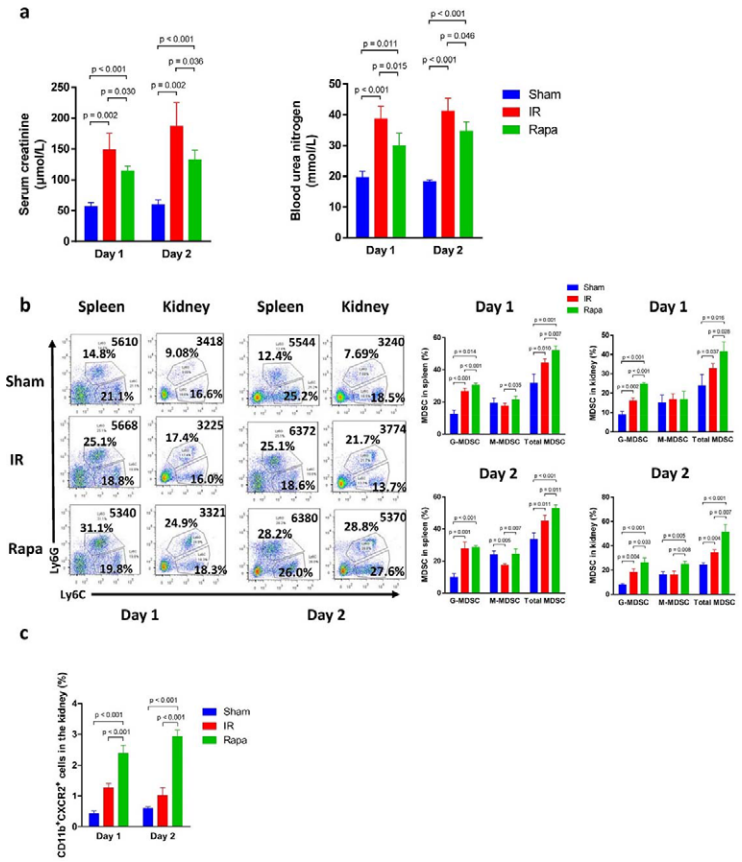
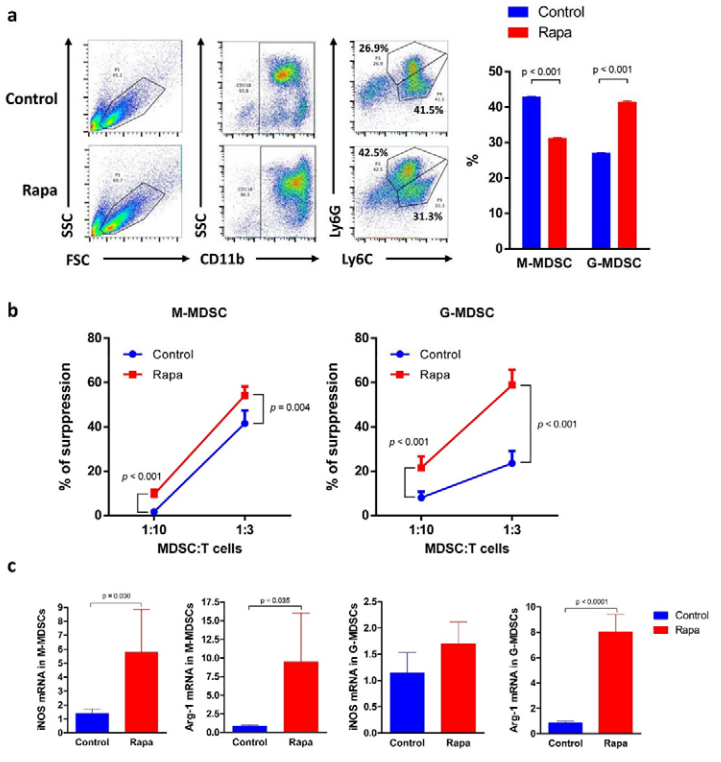


Figure 2



BOS592

SHORT, COOL AND WELL OXYGENATED – HOPE FOR KIDNEY TRANSPLANTATION IN A RODENT MODEL

Philipp Kron, Andrea Schlegel, Olivier De Rougemont, Christian Oberkofler, Pierre-Alain Clavien, Philipp Dutkowski
University Hospital Zurich, Switzerland

To investigate novel and easily applicable preservation perfusion techniques in kidney grafts obtained from donors after circulatory death (DCD).
Background: A novel perfusion approach, hypothermic oxygenated perfusion (HOPE), used for DCD liver grafts, is based on cold perfusion for 1 h by an oxygenated solution before implantation. Here, we aimed to test HOPE in a rodent model of kidney grafts associated with substantial warm ischemia.
Methods: Rat kidneys were exposed to 30 min warm ischemia, without application of heparin. Kidneys were removed and cold stored for 4 and 18 h, mimicking DCD organ procurement and conventional preservation. In additional experiments, kidneys were normothermically perfused with oxygenated blood for 1 h after cold storage. In a third group, kidneys were perfused by HOPE for 1 h after cold storage. In each group, orthotopic kidney transplantation was performed after recipient nephrectomy.
Results: HOPE treated DCD kidneys showed dramatically better function after transplantation, when compared to cold stored grafts in terms of nuclear injury, macrophage activation, endothelium activation, tubulus damage and graft function. A short period of warm oxygenated perfusion before implantation improved graft quality as compared to cold storage, but was significantly less effective in all endpoints compared to HOPE. The effect of HOPE was dependent on perfusate oxygenation in the cold.
Conclusions: HOPE of DCD kidneys was superior to other clinically used preservation approaches, consistent to earlier results in livers. Based on this, we assume a strong and generalized effect on solid organ viability by HOPE before transplantation. These results justify a clinical trial.

Translational Kidney Ischemia-Reperfusion and Preservation

BOS593

IMPROVEMENT OF GRAFT FUNCTION DURING NORMOTHERMIC EX VIVO PERFUSED KIDNEY PRESERVATION IN DONATION AFTER CIRCULATORY DEATH GRAFTS

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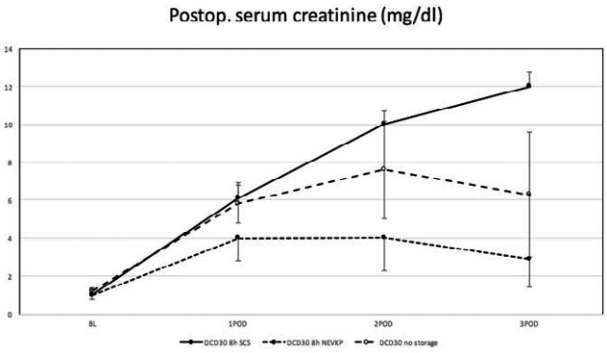
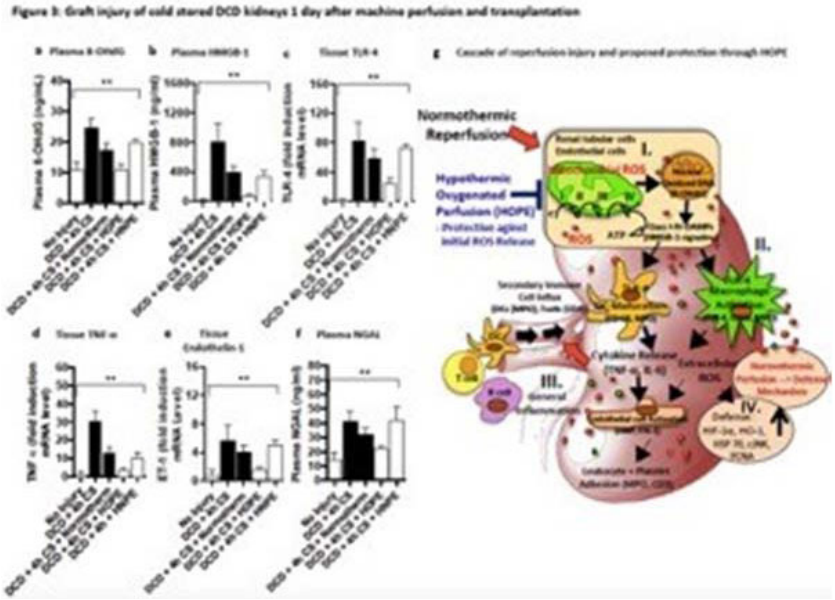


Background: Donation after Circulatory death (DCD) is an attractive strategy to increase kidney donor pool. Prolonged warm ischemic (WI) injury results severe renal graft damage with decreased postoperative function. While it has been determined that normothermic ex vivo perfused (NEVKP) preservation decreases kidney injury by reducing cold ischemic storage, the effects of NEVKP on warm ischemic injury are unknown.
Methods/Materials: We compared kidneys retrieved after 30 min WI and immediate transplantation (no preservation) with grafts that were exposed to 30 min of WI plus 8 h NEVKP or plus 8 h static cold storage (SCS) in a 3 day survival swine autotransplant model.



Results: Postoperatively NEVKP group demonstrated a lower average level of daily serum creatinine compared to no preservation group and SCS group (2nd POD: 3.9 ± 1.7 vs. 7.6 ± 2.6 vs. 10 ± 0.7 mg/dl, 3rd POD: 2.9 ± 1.5 vs. 6.3 ± 3.3 vs. 12 ± 0.8 mg/dl). Repeated measures ANOVA indicated a significantly improved early graft function in NEVKP groups compared with no-preservation ($p = 0.022$) or SCS group ($p < 0.001$).

NEVKP group had a significantly higher creatinine clearance calculated from terminal 24 h urine collection when compared to SCS or no-preservation group (NEVKP: 39.9 ± 11.74 ml/min, no-preservation 17.2 ± 10.88 ml/min $p = 0.006$, SCS: 2.7 ± 1.07, $p < 0.001$). In addition, NEVKP preserved grafts had a significantly lower grade of tubular injury and interstitial inflammation 30 min after reperfusion compared to no preserved grafts (injury score: NEVKP 1.2 ± 0.45 vs. no-preservation: 2 ± 0, $p = 0.012$; inflammation score: 0.4 ± 0.22 vs. 1.8 ± 0.84, $p = 0.002$).

Conclusion: NEVKP can be used safely to extend the organ preservation time without causing additional damage to the graft. NEVKP decreased kidney injury and improved graft function when compared to no preserved grafts. NEVKP may represent a new preservation method that promotes graft repair during preservation instead of progressing injury as it occurs with cold storage.

Clinical Kidney Ischemia-Reperfusion and Preservation

BOS594 12 YEARS EXPERIENCE USING COMBINED KIDNEY BIOPSY SCORE AND HYPOTHERMIC PULSATILE PERFUSION MACHINE TO ASSES RENAL SUITABILITY IN EXTENDED CRITERIA DONORS AFTER BRAIN DEATH

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Extended Criteria Donors (ECD) from Donors after Brain Death (DBD) require a step-wise strategy to assess kidney suitability: medical history, cardiovascular risk factors, creatinine value and macroscopic appearance. Since 2004, we introduced in ECD a combination of Kidney Biopsy Score (KBS) and renal hemodynamic evaluation with Hypothermic Pulsatile Perfusion Machine (HPPM). Accepted transplant criteria were KBS ≤ 3 & Renal Resistance (RR) ≤ 0.4 ml/mmHg/ml/min in HPPM.

Material and methods: Prospective paired kidney study of ECD-DBD, to preserve from the same donor one kidney in Cold Storage (CS) and other with HPPM (RM3 from Waters-IGL), realized between June 2004 and December 2015. End-point analysis included Primary Non-Function (PNF), delayed graft function (DGF), number of hemodialysis, hospital length in days; creatinine at hospital discharge and after 1 year.

Results: From 199 ECD-DBD generated, 81 donors were excluded (one or both kidneys not valid due to macroscopic aspect or both preserved using the same methodology, or when one kidney was only received from another center. 119 EC Donors are analysed, with 119 kidneys preserved using each methodology. No significant differences were founded between both preservation strategies, comparing sociodemographic dates, cause of death, and KBS. Only longer CIT 18.3 vs. 14.3 h (p: 0.002), because CS kidney were grafted before HPPM. Other end points not presented significant differences between methods. However, when the KBS was ≥4 & Glomerular Sclerosis ≤20%, Transplant Rate increased 19.4% after considering a RR < 0.4 as suitable organ. Comparing kidneys with KBS ≤ 3 vs. those with KBS ≥ 3: hospital length 16.26 ± 13 days vs. 25.20 ± 31 days (p: 0.027); DGF 37.3% vs. 63.6% (p: 0.004); dialysis sessions: 1.22 ± 3.03 vs. 5.79 ± 12.61 (p: 0.001) respectively. No differences were showed in creatinine.

Conclusions: Critical value for ECD acceptance is KBS, but a complementary RR allowed to increase TR and individualize decision when KBS = 4.

BOS595 PULSATIL RENAL PRESERVATION MACHINE: DEFINING THE PREDICTIVE RENAL RESISTANCE CUT-OFF VALUE FOR GRAFT FUNCTION IN OLDER UNCONTROLLED DONATION AFTER CIRCULATORY DEATH DONORS

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Hospital Clinic Barcelona, Spain

There are controversies about the predictive value of the final renal resistance (FRR) measured with Renal Pulsatil Preservation Machine (RPPM). In Uncontrolled Donation after Circulatory Death (uDCD) in our protocol we use RPPM with FRR values <0.4 mm Hg/ml/min. However, the correlation between FRR and their predictive value in the assessment of graft function has not been evaluated in uDCD.

Method : All patients who received uDCD kidney transplant between 2004 and 2016 were included. Demographic baseline characteristics of donors and recipients, FRR, cold ischemia time (CIT) are described. End-point was glomerular filtration rate (GFR) at 6 month after transplantation. Diagnostic validity for FRR was determined by COR curve, sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

Results : 194 recipients were included: 162 received kidneys from donors < 60 years old and 32 kidneys from donor ≥60 years old. In the univariate analysis, two main significant difference was found: 50% of kidneys from donors ≥60 years old presented GFR<30 ml/min at 6th months in contrast with 30% in donors <60 years old ($p = 0.05$). As well, FRR were different in both groups: 0.22 ± 0.09 vs. 0.27 ± 0.11 mmHg/ml/min respectively ($p = 0.042$). In the sample: donor ≥60 years old was divided in 2 groups based in GFR ≥ 30 ml/min: either included 16 cases with 4 never functioning grafts in the lower GFR group. Comparing both groups, a significative difference was found in FRR: 0.37 ± 0.08 in GFR<30 ml/min group vs. 0.18 ± 0.06 in GFR ≥ 30 ml/min group ($p = 0.00$). The predictive accuracy of FRR for GFR by ROC curve was 0.968 (95% CI). Consequently, the best cut-off for FRR was 0.3 mm Hg/ml /min to predict GFR at 6 months with a sensitivity of 67%, specificity of 100%, PPV of 83%, and NPV of 92%.

Conclusion: In our population FRR is a good predictor of GFR at 6 months from transplantation. Our results suggest that best cut off should be 0.3 mm Hg/ml/min for ≥60 years old UDCD.

Basic Kidney Ischemia-Reperfusion and Preservation

BOS596 COLD ISCHAEMIC KRUPPEL-LIKE FACTOR 2 DECAY IS REVERSED BY HYPOTHERMIC MACHINE PERFUSION IN A NOVEL MODEL OF HUMAN RENAL ALLOGRAFT PRESERVATION

William Ries[1], Charlotte Turnbull[1], Kamlesh Patel[2], Jay Nath[2], Thomas Smith[3], Christopher Bagnall[4], Christian Ludwig[3], Desley Neil[2], Nick Inston[2]

[1]University of Birmingham United Kingdom; [2]Queen Elizabeth Hospital, Birmingham United Kingdom; [3]Institute of Metabolism and Systems Research, University of Birmingham United Kingdom; [4]Human Biomaterials Resource Centre, University of Birmingham United Kingdom

Background: Organ preservation techniques such as hypothermic machine perfusion (HMP) involve dynamic flow of perfusion fluid across endothelium which is absent in static cold storage (SCS) conditions. The transcription factor, Kruppel-like factor 2 (KLF2), has been demonstrated to govern a panoply of flow-inducible effects and thus may facilitate a vasoprotective endothelial phenotype in perfused renal vasculature demonstrable in the environment. KLF2 expression in HMP kidneys has not been described.

This study aimed to elucidate differential KLF2 expression between kidneys in SCS and HMP conditions using deceased donor gonadal veins as a model of human allograft preservation.

Methods: Gonadal vein sections from deceased human renal allografts ($n = 6$) were divided and stored in SCS or HMP preservation for 12 h. Samples taken at baseline, 6 and 12 h were analysed by immunohistochemistry and staining objectively quantified.

Results: In SCS conditions, KLF2 expression diminished in a time-dependent manner between baseline and 12 h ($p < 0.05$). This degradation was abrogated and reversed by HMP ($p < 0.05$). At 12 h, median KLF2 expression in HMP-preserved gonadal vein samples had recovered to levels moderately elevated from baseline (13.4% increase, IQR: −52.7 to 57.9). By contrast, SCS-preserved gonadal vein expression had diminished from baseline levels by 59.4% (IQR: −86.4 to −18.4) at 12 h.

Conclusions: KLF2 degradation occurs in the static cold storage environment in the context of renal transplantation. The reversal of this decline by HMP indicates that perfusion may mediate the induction of a biochemically favourable endothelial niche, which may explain how HMP can improve outcomes following renal transplantation.

Basic Kidney Other

BOS597 A COMPARISON OF QUALITY OF LIFE OUTCOMES IN HAEMODIALYSIS PATIENTS, DECEASED DONOR AND LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS

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Background: The aim of the study was to assess differences in psychological scores between recipients of living and deceased donor kidneys, and patients on haemodialysis.
Methods: Haemodialysis patients (HDx), living donor and deceased donor kidney recipients (Rx collectively, LRx and DRx, respectively) from 2013 to 15 were asked to complete a questionnaire on life satisfaction, mood, distress and health-related quality of life (HRQoL).
Results: 296 questionnaires were completed (98 HDx, 49 LRx, 149 DRx). There was significant difference in age between HDx and Rx patients (58.4 vs. 54.0 years; $p = 0.022$), but not between LRx and DRx (51.3 vs. 55.0; $p = 0.089$). Life satisfaction and HRQoL scores were significantly lower in HDx compared to Rx ($p < 0.001$). Mood and distress scores were significantly higher in the HDx group ($p < 0.0001$ and $p < 0.001$ respectively). In the HDx group, waiting list status and living donor availability was not associated with significant differences in any of psychological scores. There was no difference in mood or distress scores between LRx and DRx groups. There was a difference in HRQoL ($p = 0.001$) and life satisfaction ($p = 0.042$), with LRx scoring better. When comparing scores between LRx, standard criteria and expanded criteria donor recipients, there was no difference in mood ($p = 0.427$) or distress ($p = 0.382$) between the 3 groups. Living donors had significantly higher HRQoL compared to both standard criteria and expanded criteria recipients ($p = 0.01$). Life satisfaction was significantly higher in the living donor cohort compared to expanded criteria recipients ($p = 0.06$).
Conclusions: This study has further quantified the psychological and health-related quality of life advantages of transplantation. The type of transplant received has no bearing on negative measures, however living donor recipients appear to score significantly higher in positive symptoms such as HRQoL and life satisfaction.

Clinical Kidney Other

BOS598 PATIENT ATTITUDES TOWARD MOBILE PHONE-BASED HEALTH MONITORING IN KIDNEY TRANSPLANTATION

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[1]Santa Casa De Juiz De Fora, Brazil; [2]Centro De Tratamento De Doenças Renais, Brazil

Background: Routine use of Mobile phone based remote monitoring of physiological parameters has the potential to transform healthcare. Not only help patients and clinicians make better decisions, but they can also enable comparisons of providers' performances to stimulate improvements in services. This technology is also relatively inexpensive, has an intuitive interface, and provides the capability for real-time personalized feedback to help motivate patient self-efficacy. There is a lack of data assessing the attitudes of renal transplant recipients toward this technology.
Methods/Materials: A cross-sectional study was conducted with transplant patients from a single transplant center institution. Patients responded a questionnaire by phone.
Results: Between October 2016 and February 2017, a total of 153 renal transplant recipients were identified and agreed to participate in the survey. The results of the survey indicate that while 93.5% of respondents own a mobile phone, but only 59.4% are smartphones. Those who hadn't a smartphone, 66.7% someone at home would have it and help. The majority of respondents, 94.7%, reported a positive attitude toward the use of a prototype system if it came at no cost. Younger patients were more likely than older patients to own smartphones (43.2 ± 14 vs. 52.2 ± 12 years of age; $p = 0.000$) and held a more positive attitude toward free use of the prototype system (45.8 ± 13 vs. 58.1 ± 14 years of age; $p = 0.002$).
Conclusions: The data demonstrates that kidney transplant recipients have a positive overall attitude toward mobile phone based health technology (mHealth). Additionally, the data demonstrates that most kidney transplant recipients own and are comfortable using mobile phones and that many of these patients already own and use smart mobile phones. Respondents were comfortable with the idea of being monitored using mobile technology and are confident that their privacy can be protected.

BOS599 EFFECTS OF VIDEO-ASSISTANT HEALTH EDUCATION ON KIDNEY TRANSPLANT RECIPIENTS: A QUASI-EXPERIMENTAL STUDY

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Background: Kidney transplantation is now a well-established treatment for end-stage renal diseases (ESRD). Proper health education can prepare and encourage kidney transplant recipients to take a better look at their health. Growing numbers of research have confirmed the effectiveness of using video as an intervention to instill ability to self-management. Therefore, the aim of this project is to develop a video-based education program for kidney transplant recipients, and assess the effectiveness of this program.
Methods/Materials: This was a quasi-experimental study. From 1 August, 2016 to 31 January, 2017, all patients who underwent kidney transplantation were recruited. Patients in intervention group were given video-based eduction before kidney transplantation, staying in Intensive Care Unit (ICU), and staying in general ward. Participants in control group received routine method in the ward. Data was collected by a researcher-made questionnaire. All statistical analyses were conducted under SPSS version 18 (SPSS Inc., Chicago IL).
Results: 163 kidney transplant recipients (intervention group = 85, control group = 78) participated in the study. There was no statistically difference between groups demographics. The mean score of perceived susceptibility, perceived severity, perceived benefit after video-assisted health education was increased and the mean score of perceived barriers was decreased. The mean of score of health literacy was also enhanced.
Conclusion: By continuous video-based health education during hospitalization, four dimensions in HBM- perceived susceptibility, perceived severity, perceived benefit and perceived barriers, are ameliorated. Health literacy is also enhanced. In general, it could be concluded that this study is evidence of positive effects of educational programs in kidney transplant patients, and the present study recommends video display as a feasible method for educating these patients based on health belief model.

BOS600 A WEB-BASED REFERRAL EXCHANGE PLATFORM: BRIDGING THE COMMUNICATION GAP BETWEEN TRANSPLANT CENTERS AND DIALYSIS FACILITIES

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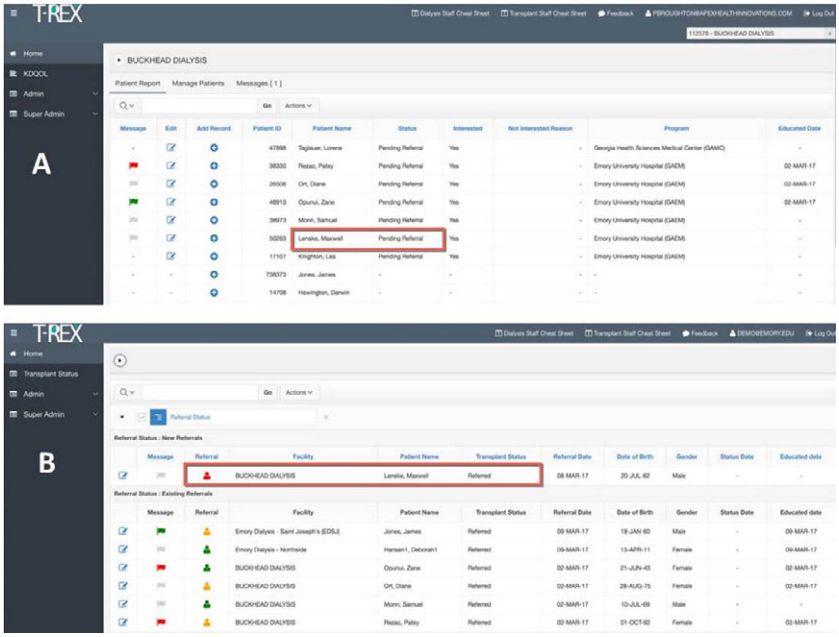
[1]Emory University, United States; [2]Apex Health Innovations, United States

Background: Managing the kidney transplant referral process from dialysis facility to transplant center is administratively intensive. Dialysis center staff need to provide and track transplant education, patient interest and barriers to transplantation, and referral (often via fax) to transplant centers. Referrals often require follow-up from transplant centers for medical evaluations and completion of medical testing to determine eligibility for the transplant list.
Methods: In 2016, we collaborated with regional stakeholders from the Southeastern Kidney Transplant Coalition and developers at Apex Health Innovations to create a multi-module, secure, web-enabled software application called the Transplant Referral EXchange (T-REX). T-REX provides a platform to electronically manage dialysis patients at all steps of the transplant process, enabling dialysis facility and transplant center staff to track the use of education materials, send/receive electronic referrals, and facilitate communications through messaging in the application.
Results: The T-REX application includes dialysis facility and transplant center facing applications for staff to upload existing patient data and to track important transplant steps. Key features of the application include: documenting the use of transplant education materials, sending/receiving an electronic referral specific to a transplant center's requirements, tracking patients' status in the transplant process, and real-time communication between staff across healthcare settings.

Conclusion: Pilot testing of the T-REX software will continue at other transplant centers and dialysis facilities in 2017 to prepare for a large, randomized controlled trial of T-REX vs. the standard of care. If found to be effective, T-REX could help improve communication between healthcare providers, streamline the efficiency of the transplant process, and ultimately help improve access to kidney transplantation for dialysis patients.



BOS601 EVALUATION OF OUTCOMES AND COMPLICATIONS OF KIDNEY TRANSPLANTATION IN PATIENTS WITH ANCA GLOMERULONEPHRITIS AS PRIMARY DISEASE

Sophia Lionaki[1], Konstantinos Panagiotellis[1], Nikolaos Altanis[1], Ilias Makropoulos[1], Apostolos Pappas[1], Alice Iniotaki[2], George Zavvos[3], John Boletis[1]

[1]Department of Nephrology & Transplantation Unit, Laiko Hospital, National & Kapodistrian University of Athens Greece; [2]Department of Histocompatibility, Gennimatas Hospital Greece; [3]Transplantation Unit, Laiko Hospital Greece

Background: ANCA associated vasculitis is an aggressive disease which often involves the kidneys and if left untreated ends up to ESRD quickly. The aim of this study was To evaluate the long term outcomes of kidney transplantation (KTx) in patients with ESRD due to ANCA-glomerulonephritis (ANCA-GN), in comparison with those of patients with primary diseases (PD) of non-autoimmune nature.
Methods: We retrospectively studied all patients with ESRD due to ANCA-GN, who received a kidney between 1995 and 2014, with a follow up of 1 year or more. Demographics, clinical, serological and laboratory data were recorded, including characteristics of the PD and the KTx. A control group, consisted of patients with PD of non-autoimmune origin, matched for age, gender, donor source, and KTx period was selected. The two groups were compared with respect to patient and graft survival and the frequency of specific complications.
Results: Of 21 patients with pauci-immune GN, 20 (95.2%) were ANCA positive at the time of PD diagnosis, 12 (60%) P/MPO-ANCA and 8 (20%) C/PR3-ANCA. 70% of them had developed rapidly progressive disease at presentation. The baseline characteristics of patients and controls at KTx are shown in Table 1.

Parameter (mean ± SD) or %	Patients with ANCA-GN *N* = 21	Control group *N* = 71	p-value
Donor age (years)	55.4 (±14.25)	53.95 (±16.6)	0.74
Time in dialysis prior to KTx (months)	78.3 (±69.6)	57 (±38.9)	0.08
Follow up (fup) post KTx (months)	81.9 (±55.6)	65.0 (±27.3)	0.06
Donor specific antibodies prior to KTx	14.3	23.9	0.35
Ser. creatinine at 1st KTx discharge (mg/dl)	1.5 (±0.4)	1.6 (±0.5)	0.13
Ser. creatinine at end of follow up (mg/dl)	1.9 (±1.4)	1.4 (±0.7)	0.03
De novo donor specific antibodies, end fup	14.3	16.7	0.79
Acute rejection (ever)	10.5	15.7	0.7
Patients? survival with functioning graft	90.5	97	0.24
Graft failure	9.5	1.5	0.14

1. *Continued*

Parameter (mean ± SD) or %	Patients with ANCA-GN *N* = 21	Control group *N* = 71	p-value
Complications post KTx (any type)	85.7	57.6	0.02
Infection requiring hospitalization	95.2	51.5	0.0004
Post KTx diabetes mellitus	9.5	13.6	0.59
Malignancy (new diagnosis)	10	4.5	0.35
Osteoporosis (new diagnosis)	9.5	24.2	0.17

95.2% of the patients with ANCA-GN and 93% of controls received anti-CD25 as induction therapy for KTx (p = 0.72), while 85.7% and 97.2% respectively (p = 0.28) were maintained with the combination of a calcineurin inhibitor, mycophenolic acid and steroids.
Conclusions: According to our results, long term graft function of patients with ESRD due to ANCA-GN, although inferior from that of patients with PD of non-autoimmune origin, it doesn't have any impact on graft survival. Infections are more frequent among patients with ANCA-GN as PD.

BOS602 ANNUAL DATA FOR KIDNEY TRANSPLANT SERVICES IN KUWAIT IN 2016

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Hamed Al-Essa Organ Transplant Center/ Ibn Sina Hospital, Kuwait

Background: Hamed Al-Essa Organ Transplant Center in Ibn Sina Hospital is the only center providing renal transplant services in Kuwait. We aimed to annually monitor and record renal transplants activities and outcome in Kuwait.
Materials and methods: Data on renal transplants were collected from hospital records from 01/01/2016 until 31/12/2016 at Hamed Al-Essa Organ Transplant center.
Results: Seventy-seven patients underwent a renal transplant in Kuwait in 2016; 53 (68.8%) patients were male and 24 (31.2%) were female. of these 77 patients, 30 (39%) received a kidney from a deceased donor, 21 (27.2%) received a kidney from a living-unrelated donor, and 26 (33.8%) received a kidney from a living-related donor. Twenty-seven (35.06%) patients were highly sensitized immunologically and underwent successful desensitization before transplant according local protocol; 15 (55.56%) of these patients were male and 12 (44.44%) were female. Five patients (6.5%) experienced biopsy proven acute rejection within the first month after transplant, 2 of them had acute rejection within one week post-transplant that led to loss of the graft in only one patient. One diabetic male patient underwent a pancreas after kidney transplant but it was unsuccessful. One hundred and one patients underwent

renal transplant outside Kuwait were added to the follow-up list in 2016; 21 of those patients had their transplants from unrelated donors without any documented legal coverage in Egypt and Pakistan; 67 (66.3%) of these patients were male and 33 (33.7%) were female. of these 101 patients, 40 patients (39.6%) received a kidney from a living-related donor, 57 (56.4%) received a kidney from a living-unrelated donor, and 4 (4%) received a kidney from a deceased donor.
Conclusions: A total of 77 patients underwent a renal transplant in Kuwait in 2016 with an acceptable success rate. Additionally, organ trafficking is an escalating health problem facing the transplant community in the Kuwait.

BOS603 IMPACT OF HEMODIALYSIS AND RENAL TRANSPLANTATION ON ERECTILE FUNCTION IN CHRONIC HCV PATIENTS WITH ESRD

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Introduction : There is a paucity of controlled studies comparing sexual health in kidney transplant recipients and end-stage renal disease (ESRD) patients on regular hemodialysis.
Aim: To investigate the prevalence of ED among HCV +ve ESRD patients and to assess effect of successful transplantation as compared to hemodialysis on improving their ED
Main outcome measures: The score and change in THE INTERNATIONAL INDEX OF ERECTILE DYSFUNCTION (IIEF-5) before and one year after dialysis or renal transplantation.
Patients and methods: The study included 78 patients with HCV +ve ESRD Patients were divided into two groups: 48 patients on regular hemodialysis, assessed before & one year after start of hemodialysis and 30 patients who were candidates for RT, assessed for ED before and 1 year after successful RTx. All patients were subjected to full medical and sexual history then filled the International Index of Erectile Function (IIEF-5) questionnaire.
Results: There was a significant difference in IIEF before and after dialysis (6.88 ± 0.030 before and 8.48 ± 5.842 after, $p < 0.035$). There was a mild significant negative correlation to age before dialysis ($p < 0.005$) and highly significant strong negative correlation after dialysis ($p < 0.0001$). On the other hand, there was a highly statistically significant difference between IIEF before and after RT (17.13 ± 2.446 before and 21.90 ± 3.284 after, $p < 0.0001$). There was a non-significant negative correlation to age before RT ($p < 0.249$) but high negative correlation after ($p < 0.0001$). The study showed no statistical correlation between improvement in both IIEF post dialysis & post RT and the pretreatment score. There was a better improvement in erectile function in RT patients compared to hemodialysis treatment.
Conclusion: Erectile dysfunction is an extremely common problem in HCV.

BOS604 THE REASONS FOR PATIENTS' PREFERENCE AMONG RENAL TRANSPLANT PATIENTS

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Background: The optimum treatment of end-stage renal disease is renal transplantation. In contrast to the worldwide trend, living donor renal transplantation is being popular approach in Turkey. In our country, renal transplantation is performed in many centers with successful results. We aimed to demonstrate the possible factors associated with the patients' preference for transplantation centers.
Method: 220 patients who were examined in nephrology outpatient clinic for preparation for renal transplantation were asked for preference of renal transplant center through the donor coordinator survey.
Results: The characteristics of patient is summarized on Table 1. The questions of survey and the comparison between the preference of general and private hospital is demonstrated on Table 2. The possibility of cadaveric transplantation, living of parents and relatives and being of the transplantation center in the same city and ease for the postoperative follow-up was found the possible factors associated with the preference of general hospital in univariate analyses. Most experience in living donor and cross donor transplantation, physical condition of center, friend-doctor advisement for the possible center, the usage of extended transplantation criteria and short preoperative preparation time was the possible associated factors for the preference of private hospital. In the preference of general or private hospital, age, gender, education status, job, presence of preoperative dialysis treatment programme, advertisement of transplant center, hospitality of center and long term transplant organ function of transplanted patients did not demonstrate statistical significance on univariate analyses.
Conclusion: We are able to demonstrate the possible factors associated with the preference of centers by the patients. Each type transplant center (private or general) has a few superiority to the other depending on our survey study.

BOS605 ABO-INCOMPATIBLE (ABOI) LIVING DONOR WITH KIDNEY TRANSPLANTATION: STUDY OF 38 PATIENTS

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Background: ABO-incompatible (ABOi) living donor with kidney transplantation (LDKT) has been used in the last few years under different conditioning protocols, with good results. The present study describes the results obtained this technique in our hospital during the period 2008–2016.
Methods: Thirty-eight patients with a mean age of 50.1 ± 10.6 years (18 on dialysis) were included. The duration of follow-up was 31.98 ± 24.7 months. Conditioning: rituximab (RTX) 375 mg/m^2, tacrolimus, mycophenolate mofetil (MMF) or mycophenolate sodium (MFS), prednisone, plasmapheresis (PPS) /

Demographics	Total	General hospital	Private hospital
Male/Female	77/143	60/108	17/35
Single/Married/Divorced	60/158/2	49/118/1	11/40/1
Literate/not literate	10/12	8/10	2/2
Primary/high school/University graduated	124/46/28	95/34/21	29/12/7
Full time job/no job/part time job	56/144/20	45/107/16	11/37/4
Hemodialysis/peritoneal dialysis/no dialysis	150/30/17/23	116/25/10/17	34/5/7/6
Living donor/cadaveric donor	174/46	125/43	49/3
Relative/no relative/ cross	165/4/4	125/0/0	40/4/4

	Absolutely yes	yes	Partially yes	no	Absolutely no	p Value
Advised any transplanted patient	12/7	40/17	4/1	109/26	3/1	0.042
Impact of media advertisement	2/0	11/7	5/2	147/42	3/1	NS
Simple transportation	70/4	63/12	12/4	23/31	0/1	0.000
Short transplant preparation	6/3	18/20	96/24	45/4	3/1	0.000
Advanced physical condition of center	12/3	77/34	37/12	38/3	4/0	0.01
Experience of transplant team	27/8	80/26	10/2	48/15	3/1	NS
Number of transplantation of center	8/3	64/24	19/2	75/22	2/1	NS
Hospitality of center	24/6	112/34	13/0	18/5	1/2	NS
Advice of another doctor	34/6	73/2	2/0	54/22	5/2	NS
Ease of postop follow up	76/4	71/16	12/4	9/27	0/1	0.00
More cadaveric transplant	5/1	9/2	10/1	141/46	3/2	NS
Long term transplant organ function	10/1	28/11	24/6	103/34	3/0	NS
The usage of extended transplantation criteria	9/5	12/16	7/6	137/25	3/0	0.000
Recommendation of this center to another patient	40/7	105/36	7/0	9/9	1/0	0.01
Cross transplant experience	0/5	1/5	0/0	128/33	39/9	0.000

immunoadsorption (IA) and intravenous immunoglobulin (IgIV). Accepted IgG and IgM titers for transplantation ≤1/8, determined with gel card techniques.
Results: Preprocess IgG titer 1/117 ± 1/150, IgM titer 1/88 ± 173. After 6.57 ± 3.5 sessions, IgG decreased to <1/8 in 37 patients and to <1/16 in one. IgM was < 1/8 in all cases. Eighteen patients (47%) presented hematoma, with a need for reintervention in 5 (13.2%); 22 (58%) required transfusion. Acute rejection occurred in 4 cases. CMV infection was observed in 5 cases, BK viremia in 3, post-transplant diabetes in 9 and lymphocele in 3. Patient survival was 100% and graft survival 94.5% after one and 3 years. Creatinine concentration was 1.5 ± 0.5 mg/dl after one year and 1.49 ± 0.44 mg/dl after 3 years. Proteinuria was 0.3 ± 0.3 g/24 h after one year and 0.29 ± 0.29 g/24 h after 3 years.
Conclusions: In our experience, ABOi-LDKT after conditioning with RTX, PPS/IA and IgIV is a valid option offering excellent outcomes. An increased tendency towards postoperative bleeding is observed.

BOS606 OUR STRATEGY TO PROMOTE A MEDICAL SYSTEM FOR RENAL TRANSPLANTATION IN REMOTE ISLANDS AND RURAL AREAS IN NEAR FUTURE; EXPERIENCE IN OUR CENTER

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Background: Okinoerabu Island and Tokunoshima Island lie in the sea to the south of the Japanese mainland, about 100 km north of Okinawa and about 500 km south of Kyushu. There are no facilities that specialize in kidney transplants, so the patients need to leave the island to undergo the procedure. Up to a few years ago, there were less than 5 kidney transplant patients on the island. Recently, likelihood of kidney transplantation has been much higher among these islands. The number of transplant patients has gradually increased. We report the status of transplant medicine on these remote islands, including concrete methods for periodic examinations and how emergencies are handled.
Patients and methods: Recipient age was 60.0 ± 8.9 years (mean ± SD); 15 were males and 10 were females. Donor age was 57.9 ± 8.48 years (mean ± SD); 14 were males and 11 were females. Recipient diseases leading to ESRD were diabetes (36.0%), chronic glomerulonephritis (28.0%), and ADPKD (12.0%). The duration of dialysis prior to transplantation was 382.6 ± 233.2 days (mean ± SD).
Results: We physicians specializing in kidney transplants formed an alliance with local facilities a few years back to create specialized outpatient facilities. Delayed graft function was observed in only 1 patient, biopsy-proven acute rejection in 4 patients, and chronic allograft nephropathy in 2 patients. In these cases, the local doctor performed the treatment in their facilities under our direction. Most of the treatments were performed safely and successfully. None of the patients has had graft loss, with mean SCr (serum Cr level) of 1.35 ± 0.85 mg/dl.
Conclusions: To coordinate medical care recipients with their primary care physicians, physicians specializing in kidney transplants no longer need to travel long distances to receive follow-up outpatients. Our approach could be an effective way to promote a medical system for renal transplant surgery on other remote rural island regions in the near future.

BOS607 MEDIUM-TERM OUTCOMES OF ABO-INCOMPATIBLE LIVING KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Background: Kidney transplantation is the optimal and most effective treatment for end-stage renal disease (ESRD). However, a severe donor shortage means that many patients with ESRD are on a waiting list. Especially, in Japan, deceased organ donation is limited and to overcome this profound donor shortage, ABO-incompatible kidney transplantation (ABO-i KTx) has flourished since the 1990s. Since 2005, a new protocol including anti-CD20 monoclonal antibody (rituximab) without splenectomy was introduced in Japan. The new protocol for ABO-i KTx was started since April 2009 in our institute.
Material/methods: Between April 2009 and January 2017, 141 living kidney transplantations were performed at Ohkubo Hospital. Among 41 patients who underwent ABO-i KTx were analyzed retrospectively. The immunosuppressive protocol, consisting of tacrolimus, mycophenolate mofetil and methylprednisolone, was started 1 week prior to the operation. All the patients received induction therapy with basiliximab. The preconditioning protocol included 1–3 sessions of plasmapheresis and a single dose of rituximab before the operation. We assessed medium-term outcomes of ABO-i living KTx.
Results: All patients underwent ABO-i KTx successfully. The 2-year patient survival rate was 100%, and the 2-year graft survival rate was 96.7%. None patients experienced clinical or subclinical AMR within 2 years. Two patients lost the graft. One patient lost the graft due to severe acute TMR 2 years after KTx. And the other patient lost the graft due to C-AMR after 5 years KTx. Excluding two recipients who lost the graft, the current mean serum creatinine levels were 1.34 mg/dl.
Conclusions: Recently, protocol including rituximab developed to allow to undergo ABO-i KTx successfully without splenectomy. And, the outcome is comparable that of ABO-compatible KTx.

BOS608 QUALITY OF LIFE IN SUDANESE RENAL TRANSPLANT PATIENTS: WHO IS BENEFITING?

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Background: Quality of life (QoL) has become an important focus of patient care and clinical outcome research. Renal transplantation program in Sudan has been running for over 15 years However no formal assessment of QoL of Sudanese renal transplant recipients has been made. In addition, very limited data come from Sub-Saharan Africa about QoL of renal transplant recipients.
The aims of these study were to evaluate the QoL in a cohort of kidney transplant recipients in Sudan, with specific emphasis on physical, social and psychological domains.
Methods: Forty patients were interviewed in this pilot study. A validated Arabic translated version of form SF-36 was used to assess the patients' QoL. Patients interviewed were those attending the transplant clinic at Sharg El-Neel and Ahmed Gasim Hospitals, Khartoum State, Sudan. Inclusion criteria included those patients who were at least one year post-renal transplantation and patients above 18 years of age.
Results: All patients scored 100% in social functioning domain. However, the scores in the psychological and physical domains were not as high. There was a statistically significant difference between males and females in all three tested domains as males scored higher than females (=0.001). There was statistically significant association between QoL and employment status (=0.048) and a strong trend between QoL and employment status (=0.058).
Conclusion: Renal transplantation resulted in significant improvement in QoL, especially in social domain. However, this improvement in QoL was more evident in males, patients with higher educational level and those in employment. The final result of this ongoing study will be awaited.

BOS609 THE LONG-TERM OUTCOME OF RENAL TRANSPLANTATION IN PATIENTS WITH LUPUS NEPHRITIS AMONG EGYPTIAN POPULATION: SINGLE CENTER EXPERIENCE

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Background: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease affects multiple organs with clinically heterogeneous outcomes.

Figure (1) : Graft survival :

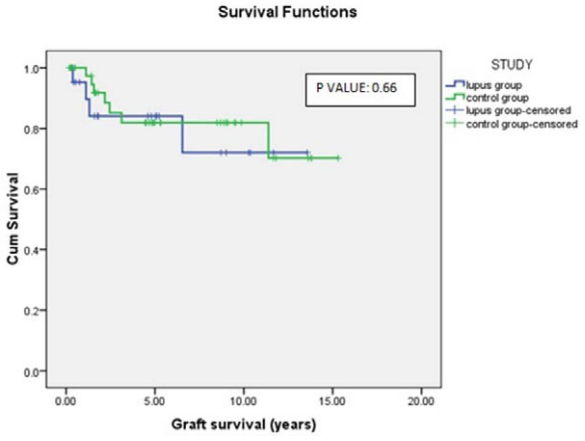
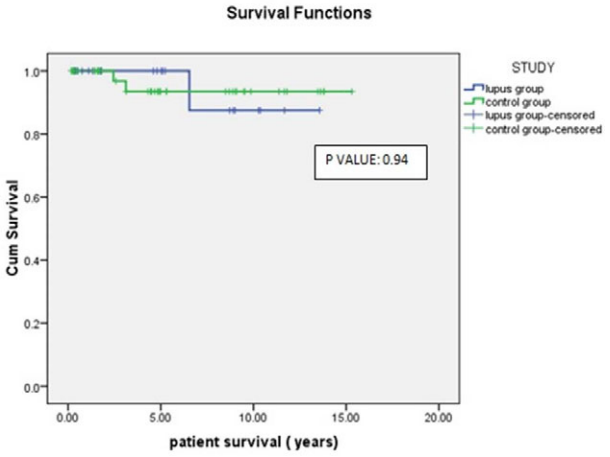


Figure (2): patient survival :



Lupus Nephritis (LN) is a common complication of systemic lupus erythematosus, and it occurs in 31–65% of SLE patients. kidney transplantation is the best long-term option for patients with End Stage renal Disease. The aim of this work is then to assess the patient and graft outcome for those who reached end stage renal disease and received kidney transplantation at urology and nephrology center, Mansoura University.
Subjects and methods: The material of this section include 23 kidney transplant recipients due to lupus nephritis. A 46 matched kidney transplant patients who were diagnosed as end stage renal disease due to other causes will serve as control group.
Results: Results of the study showed no difference in patient and graft outcome between kidney transplant recipients due to lupus nephritis and kidney transplant recipients due to other causes. The risk of recurrence of lupus nephritis in the graft is very low if compared with FSGS or MPGN.
Conclusion: se concluded that kidney transplantation for lupus patients is safe and carries no risk for lower patient or graft survival. The risk of recurrence is much lower if compared with other glomerular diseases.

BOS610 PREGNANCY AFTER RENAL TRANSPLANTATION: A MULTI-CENTER EXPERIENCE

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Background: Pregnant women with renal allografts often face several complications such as pregnancy induced hypertension, chronic deterioration of graft function and increased risk of preterm delivery. We examined women with renal transplants who became pregnant and delivered at our hospital group.
Methods: of 67 women who underwent renal transplantation between 1973 and 2015 and became pregnant and delivered at Osaka University Kidney Transplant Group Hospitals, 60 women with complete data served as subjects.
Results: Mean recipient age at the time of transplantation was 26.8 years (10–38). Mean duration from transplantation to delivery was 6.0 years (1.6–15.3). Calcineurin inhibitors comprised the immunosuppressive therapy in 45 recipients (75%). 12 recipients delivered twice and 2 recipients delivered twins. As a result, a total of 74 neonates were delivered. Mean gestational period was 36.4 weeks (25.6–41.0), and mean birth weight was 2438 g (608–3730). Intrauterine growth retardation was observed in 10. One child with intrauterine growth retardation died at 3 months old due to respiratory distress syndrome. Congenital malformations were observed in four neonates (5.4%). Prevalence of pregnancy induced hypertension was 29%. In 10 of the 72 deliveries (14%), renal function exacerbated after delivery. Rates of graft survival for the 60 recipients at 1, 5 and 10 years after delivery were 100%, 90% and 71%, respectively. Prognosis for renal transplant is significantly poorer for recipients with hypertension prior to pregnancy than for recipients without hypertension (log-rank test, $p = 0.026$).
Conclusions: Rates of graft survival after delivery were mostly favorable. In patients with drug-treated hypertension prior to pregnancy, subsequent renal function may be adversely affected.

Clinical Kidney Cardiovascular Complications

BOS611 THE ASSOCIATIONS BETWEEN SODIUM INTAKE AND KIDNEY DAMAGE WITH ECHOCARDIOGRAPHIC PARAMETERS IN RENAL TRANSPLANT RECIPIENTS

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In present study we aimed to evaluate the associations between graft function, urinary sodium and protein excretions and echocardiographic parameters in stable renal transplant patients.
Materials and methods: Two hundred and fifty-nine renal transplant recipients (154 male, mean age: 42.6 ± 11.6 years) with stable allograft function were evaluated cross-sectionally. All patients were evaluated for clinical, biochemical parameters, 24-h urinary sodium excretion (24-h UNa) and protein excretion (24-h Upr). Pulse wave velocity (PWv) was determined from pressure tracing over carotid and femoral arteries. Left ventricular end diastolic pressure (LVED) and left ventricular mass index were reported. According to 24-h UNa patients were divided into 2 groups as group 1 (24-h UNa ≥ 100 mmol/l; *n*: 98) and group 2 (24-h UNa < 100 mmol/l; *n*: 161).
Results: The median 24-h Upr was 250.0 (242.5) mg/day, the mean 24-h UNa was 169.0 ± 72.3 mg/day, mean LVMI 96.1 ± 33.1 g/m^2 and the mean LVED was 4.46 ± 0.5 mm Hg. In correlation analysis, LVMI was positively correlated with LVED (r: 0.731, p: 0.001), Upr (r: 0.283, p: 0.0015), UNa (r: 0.226, p: 0.001), PWv (r: 0.339, p: 0.005) and negatively correlated with serum albumin levels (r: −0.0416, p: 0.0003). The mean Upr in group 1 was 214.9 ± 10.4 and 71.1 ± 8.8 mg/day in group 2. LVED (4.6 ± 0.09 vs. 4.2 ± 0.13 mmHg, p: 0.001), LVMI (108.5 ± 7.1 vs. 81.0 ± 9.1 g/m^2, p: 0.008), Upr (340.1 ± 28.8 vs. 230.1 ± 26.9, p: 0.049) levels were higher in group 1. In linear regression analysis, LVED (p: 0.011) and serum albumin (p: 0.009) were detected as the predictors of LVMI.
Conclusion: By this trial, we found that that increased urinary sodium intake leads to increased risk of cardiovascular events in renal transplant recipients. Moreover, higher sodium intake may be an additional insult to chronic allograft disfunction leading increased proteinuria; therefore limiting sodium intake should be an important goal in the follow-up of this group.

Clinical Kidney Metabolic Complications

BOS612 THE TREND IN WEIGHT GAIN AFTER KIDNEY TRANSPLANTATION IN PRE-TRANSPLANT NON-OBESE PATIENTS

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Background: Obesity is one of the main contributing factors of poor kidney transplant outcomes. Weight gain after kidney transplantation is common, but the consequence of pre-transplant obesity on post-transplant weight gain is unclear.
Methods/Materials: Kidney transplant recipients over the past 1 year was followed up during post-transplant period. The patients were stratified into 2 groups depending on pre-transplant body mass index (BMI): non-obese and obese groups if the patients had BMI <30 or ≥30 kg/m^2, respectively. Increase in BMI of each groups was compared over 24 months.
Results: Among 70 kidney transplant recipients during the study period, mean age was 52.66 ± 1.43 (SEM) years and two-third was male (41 patients; 59%). Mean BMI was 27.64 ± 0.67 kg/m^2. Forth-eight patients were non-obese with mean BMI of 24.69 ± 0.5 kg/m^2, and the remaining 22 patients were obese with mean BMI of 34.08 ± 0.81 kg/m^2. During 24 months follow-up, 93.7% of patients in non-obese group gained weight with the estimated median time of weight gain of 11.43 ± 1.73 weeks post-transplantation (95% CI 8.034 – 14.82); whereas, the number of patients who gained weight was lower in obese group (81.8%) and the estimated median time of weight gain slightly delayed up to 14.71 ± 1.84 weeks post-transplantation (95% CI 11.10

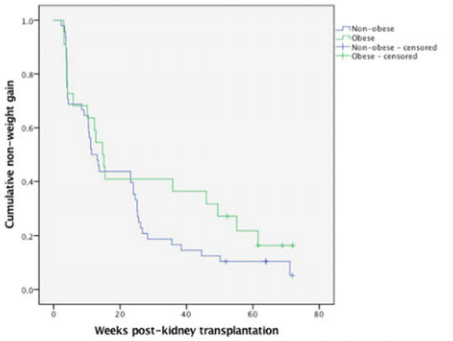

Figure 1: Kaplan-Meier curve of distribution of increase in body mass index during 24 months post-kidney transplantation in pre-transplant non-obese (blue curve) and obese (green) groups.

– 18.33). The distributions of increase in BMI of non-obese and obese groups were compared and difference between these 2 groups were statistically insignificance, $\chi^2 = 1.382$, p-value of 0.240 (log rank test, Fig. 1).
Conclusion: More patients with pre-transplant non-obesity appear to gain weight in a shorter period of time during post-transplantation compared to pre-transplant obese patients. Since obesity continues to convey poor outcomes after kidney transplantation, losing weight and preventing weight gain should be implemented in not only pre-transplant obese patients, but also pre-transplant non-obese patients.

BOS613 POST TRANSPLANT DIABETES MELLITUS (PTDM) IN KUWAIT

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Hamed Al Essa Organ Transplant Center, Kuwait

Introduction: Diabetes mellitus (DM) is considered the second leading cause for chronic kidney disease (CKD) in Kuwait (24%). Kidney transplantation is the treatment of choice for patients with CKD. PTDM is a known entity that can affect graft and patient survival.
Patients and methods: We conducted a survey analysis for prevalence of DM among kidney transplant recipients (KTR) who were following up in our Center. A questionnaire involving patients' demographic data, type of diabetes and known risk factors for PTDM was attached to all patients' records in outpatient department (OPD) and filled up by the attending physician. The data were collected in Excel sheet and analyzed by the SPSS software.
Results: We reviewed 1389 KTR over 6 months from April to September 2015. There were 48 (3.5%), 301 (21.7%) and 356 (25.6%) patients labeled as type I, type II and PTDM respectively and remaining 684 (49.2%) patients were non-diabetics (ND). Almost 57.9% of KTR with PTDM were in the middle age group with mean age of 49.48 years ($p = 0.0001$). There were more patients with physical inactivity in PTDM group compared to ND ($p = 0.008$). Body mass index was significantly higher in PTDM compared to ND groups (29.8 vs. 28.3% respectively) $p = 0.008$. When we compared the known risk factors for PTDM we found that having cardiovascular disease ($p = 0.0001$), perioperative hyperglycemia ($p = 0.0001$), human leucocyte antigen B (HLA-B) mismatch ($p = 0.023$) and male sex ($p = 0.04$) were associated with development of PTDM. According to level of education, illiteracy was associated with significant increase in PTDM ($p = 0.002$) compared to school or higher education. Type of immunosuppression didn't have impact on development of PTDM ($p > 0.29$).
Conclusion: PTDM has a major contribution to the diabetic pool in our center. Risk factors for PTDM are similar to those for diabetes in the general population.

BOS614 CHOLESTEROL AS AN INDEPENDENT PREDICTOR OF OUTCOME AFTER RENAL TRANSPLANTATION

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Introduction and aims: Many studies have demonstrated a logistic relationship between serum cholesterol levels and the incidence of coronary-vascular diseases. In patients with a renal graft hyperlipidaemia occurs in 60–80% and cardiovascular death in 40–60% of the patients. In patients with a renal graft myocardial infarctions occur 25 times more often compared to the normal population. In spite of this, there is still discussion whether renal transplant patients with high serum cholesterol levels should be treated, as there is no conclusive evidence of a direct relationship between serum cholesterol level and cardiovascular death in this multi-risk patient population.

Our aim is to study the effect of serum cholesterol, as a continuous variable, on long-term graft, patient and over-all graft survival.
Materials and methods: At the University Hospital Center "Mother Tereza" and American Hospital 150 kidney-transplantations were performed from the start in 2007 until January 2015. The analysis was done in January 2007, all patients having at least 5 years of follow-up. To evaluate the long-term risk factors we studied those patients that were alive with a functioning graft, one year after transplantation ($n = 100$). Serum cholesterol, creatinine and data regarding the presence of proteinuria and hypertension between one and two years after transplantation were gathered. Hypertension was defined as a diastolic blood pressure above 90 mm Hg and/or a systolic blood pressure above 140 mm Hg at two or more visits, or the use of antihypertensive medication. Proteinuria was defined as urinary protein excretion above 0.15 g/l at more than 2 visits. Patients were not routinely treated with cholesterol lowering medication.
Results: In the Cox proportional hazards analysis serum cholesterol at one year after transplantation turned out to be an important, independent variable influencing all end points (adjusted for all other variables in the model). The influence on graft failure censo.

BOS615 METABOLIC COMPLICATIONS IN HIV-INFECTED KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Renal transplantation is now a viable option in HIV-infected patients. Post transplantation, metabolic complications may occur, as dyslipidemia, diabetes mellitus, hypertension etc. Corticoids, calcineurin inhibitors, antiretroviral therapy and HIV infection itself may be involved in promoting post transplant metabolic complications.
Methods: We studied 24 HIV-infected kidney transplant (KT) recipients, transplanted in the Pitié- Salpêtrière Hospital in Paris, France in the period January 2004–December 2015. They were matched to 21 noninfected KT recipients, transplanted in the same center in the same period.
Results: Pre transplantation, incidence of diabetes mellitus was 13% in HIV-infected KT recipients and 10% in the control group ($p = 0.36$). All patients received insulin treatment. Post transplantation, incidence of diabetes mellitus was 38% in HIV-infected KT recipients, similar to HIV-negative controls (58%, $p = 0.18$). A percentage of 78% of HIV-infected KT recipients and 58% of controls received insulin treatment. Before and after transplantation, 58% of HIV-infected KT recipients and 43% of controls had hypertension ($p = 0.23$).

Lipid profiles pre and post transplantation are described in Table 1. Lipid profiles were similar between HIV-infected patients taking protease inhibitors, nucleoside reverse transcriptase inhibitors, non nucleoside reverse transcriptase inhibitors and integrase inhibitors. All patients had good immunovirological control, with undetectable viral loads and CD4 over 200 cells/mm^3.

Cardiovascular events (myocardial infarction, cerebrovascular accident) were equally frequent in the two groups (4% vs. 5%, $p = 0.9$).
Conclusions: Incidence of pre and post transplant diabetes and hypertension as well as lipid profiles are similar in HIV-infected KT recipients and HIV-negative controls.

	HIV-infected KT recipients	HIV-negative KT recipients	p value
LDL-c pretransplantation (mg/dl)	116 (88–175)	95 (73–147)	0.38
LDL-c at 3 month post KT (mg/dl)	102 (90–133)	110 (87–152)	0.78
LDL-c at 1 year post KT (mg/dl)	100 (78–153)	117 (90–154)	0.89
HDL-c pretransplantation (mg/dl)	53 (40–77)	59 (49–66)	0.90
HDL-c at 3 month post KT (mg/dl)	77 (44–95)	68 (59–84)	0.91
HDL-c at 1 year post KT (mg/dl)	67 (51–75)	45 (41–115)	0.79
TG pretransplantation (mg/dl)	168 (109–176)	110 (86–231)	0.66
TG at 3 month post KT (mg/dl)	100 (82–201)	160 (113–221)	0.13
TG at 3 month post KT (mg/dl)	78 (52–206)	103 (81–127)	0.73

BOS616 INCIDENCE OF DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION IN SLOVAKIA – MULTICENTRIC PROSPECTIVE ANALYSIS

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Initial examinations	Hazard ratio	95% CI	p Value
Age at the time of KT < 50 years	0.4469	0.1877–1.0640	0.0688
Age at the time of KT 50–59 years	2.6020	0.9083–7.4542	0.0749
Age at the time of KT ≥ 60 years	0.3871	0.1659–0.9033	0.0281
Positive family history for DM2	0.7987	0.5391–1.7767	0.5817
Waist at the time of KT >94 cm (males), >80 cm (females)	3.4833	1.2789–9.4878	0.0146
BMI at the time of KT < 25 kg/sqm	0.4882	0.1925–1.2383	0.1311
BMI at the time of KT 25–29.9 kg/sqm	1.0670	0.4749–2.3974	0.8751
BMI at the time of KT ≥ 30 kg/sqm	3.0011	1.0725–8.3977	0.0363
C-peptide at the time of KT >5 ng/ml	1.6798	0.7228–3.9041	0.2280
IRI at the time of KT >23 μU/ml	1.6356	0.4612–5.8010	0.4462
Triacylglycerols at the time of KT >1.7 mmol/l	2.9763	1.0141–8.7352	0.0471
Cholesterol at the time of KT >5.16 mmol/l	1.4151	0.6376–3.1407	0.3933

Introduction: The incidence of posttransplant diabetes mellitus (PTDM) after kidney transplantation (KT) is 5–40%. The objective of the analysis is to identify the risk factors of PTDM after KT in the Slovak Republic (SR).
Materials and methods: In the group of 133 patients/non-diabetics, we identified the risk factors of PTDM in the monitored period of 12 months from transplantation.
Results: The incidence of PTDM in the SR in 2014 was 38.3%. By logistic regression, we discovered that the age at the time of KT [odds ratio 1.0885; 95% CI 1.0222–1.1592 (p = 0.0082)], the value of body mass index at the time of KT [odds ratio 1.4606; 95% CI 1.0099–2.1125 (p = 0.0442)], and the value of insulin resistance index (HOMA-IR) at the time of KT [odds ratio 2.5183; 95% CI 1.7119–3.4692 (p < 0.0001)] represent predictive factors of PTDM. The independent risk factors of PTDM in our group are: age at the time of KT of more than 60 years [HR 0.3871; 95% CI 0.1659–1.7767 (p = 0.0281)], waist circumference at the time of KT in males more than 94 cm and in females more than 80 cm [HR 3.4833; 95% CI 1.2789–9.4878 (p = 0.0146)], BMI at the time of KT [HR 3.0011; 95% CI 1.0725–8.3977 (p = 0.0363)], and triacylglycerols at the time of KT more than 1.7 mmol/l [HR 2.9763; 95% CI 1.0141–8.7352 (p = 0.0471)] – Table 1.
Conclusion: In the group of Slovak patients after kidney transplantation, the dominating risk factor for PTDM development is insulin resistance prior to KT.

BOS617 HYPERAMMONEMIA DUE TO LATE ONSET OF UREA CYCLE DISORDER AFTER KIDNEY TRANSPLANT CAUSING SEVERE BRAIN EDEMA AND DEATH: A CASE REPORT

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Severe hyperammonemia is a life threatening condition that can present at any age. If not treated it could cause toxic brain damage and even death. Very few cases of hyperammonemia in post kidney transplant were reported. We present a case of a 56 years old male who had deceased donor kidney transplant with initial delayed graft function that gradually recovered. Kidney biopsy did not show rejection and kidney Doppler always showed patent vessels. Two weeks postoperatively, he developed decreased conscious level that required tracheal intubation. Laboratory studies at admission to the intensive care unit showed severe hyperammonemia 660 μmol/l with normal liver function tests. Despite aggressive treatment of hyperammonemia, the patient's condition continued to deteriorate. He developed status epilepticus that did not respond to multiple medication. Ct brain progressed from normal to severe brain edema within 2 days. The causes of hyperammonemia were thoroughly investigated. Liver imaging and labs did not show liver disease. The patient was on daily hemodialysis, then on continuous hemodialysis. Infective etiology was ruled out and patient was on broad spectrum antibiotics. Late onset urea cycle disorder was highly suspected and amino acids level were tested. Glutamine, Phenylalanine and Ornithine were elevated, while most other amino acids were low. Further diagnostic test of urea cycle disorders could not be performed. Late onset of urea cycle disorder can be triggered by several factors of stress including: surgery, steroids, infection, etc. Unexplained deterioration of conscious level post kidney transplantation could be related to high ammonemia due to late onset of urea cycle disorder.

Basic Kidney Metabolic Complications

BOS618 PREVALENCE OF DIABETES MELLITUS AMONG KIDNEY TRANSPLANT RECIPIENTS IN KUWAIT; DATA OF 2015

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Introduction: State of Kuwait is one of the top 10 countries for the prevalence of diabetes mellitus (DM) worldwide (20.7% in year 2011). Diabetes is considered as the second cause (24%) of renal failure in Kuwait. Prevalence of diabetes among kidney transplant recipients (KTR) is not recently estimated.
Patients and methods: We did survey analysis for 1392 KTR who were actively following up in our center till September 2015. A survey questionnaire was distributed in patients' files during their visit to the treating physician in the outpatient department. The survey questionnaire included basic patients' demographic data, type of diabetes, medical comorbidities and known risk factors for post transplant diabetes.
Results: Out of the 1389 surveyed KTR, 48 (3.5%) had type I DM, 301 (21.7%) had type II DM and 356 (25.6%) had post transplant DM (PTDM). The remaining 684 (49.2%) were non-diabetic. The total number of diabetic patients (n = 705) exceeded half of KTR (50.8%), majority of them (92.6%) were of Arab nationality. According to our old estimation in 1998, the prevalence of diabetes among KTR was 33.7%, 12.5% had pretransplant DM and 21.2% had PTDM. The prevalence of diabetes among Kuwaiti nationals in the current study is 53.8% compared to 43.7% in other Arab nationalities and 49.5% in non-Arabs. The mean age (53 vs. 38 years old) and the number of patients aged 45 years or above (75.6% vs. 32.6%) were significantly higher in diabetic compared to non-diabetic KTR respectively [p = 0.0001]. Diabetes was steadily increasing through all age groups starting from pediatric to very old age with significant difference [p = 0.0001]. There was no difference in gender (63.5% vs. 64.4% for males) [p = 0.38] but the educational level was lower in diabetic compared to non-diabetic KTR [p = 0.0001].

Clinical Kidney Metabolic Complications

BOS619 HYPERURICEMIA FOLLOWING RENAL TRANSPLANTATION: A 3-YEAR CLINICAL RESULTS

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Introduction: In kidney transplant recipients (KTR), hyperuricemia (HU) is a commonly observed phenomenon, due to both calcineurin inhibitors (particularly cyclosporine A) and reduced kidney allograft function. The association of elevated uric acid (UA) level and kidney transplant graft function/failure still remains controversial.
Objective: We conducted a retrospective study to determine the prevalence of HU, its risk factors and graft function/survival according UA level among KTR.
Material and methods: A total of 138 patients were included in the study. We used univariate analyses to compare clinical and demographic data between the hyper- and normouricemic groups. We used multivariate adjusted logistic regression to detect independent predictors of HU. Hyperuricemia was defined as serum uric acid level of >416 μmol/l (7 mg/dl) in men and of >357 μmol/l (6 mg/dl) in women or xanthine-oxidase inhibitors use.
Results: The patients had a mean age of 46.6 ± 13.9 years and a median posttransplantation time of 3.4 years. The prevalence of HU was 42.4% (n = 61). There was a significant relationship between HU and graft loss (p = 0.031). Multivariable analysis using a logistic regression model showed the following to be independent predictors of HU: increased body mass index (OR 1.90; p = 0.042), reduced eGFR in 24 month after kidney transplantation (OR 1.32; p = 0.041), cystic kidney diseases (OR 4.95; p = 0.001), diuretics and RAS inhibitors use (OR 2.68; p = 0.025 and OR 2.22; p = 0.018, accordingly) and graft loss as well (OR 5.25; p = 0.031). Kaplan–Meier graft survival curve was significantly (p = 0.027) lower in HU group than that of normouricemic group.

Conclusions: Hyperuricemia is a common complication after kidney transplantation. Risk factors associated with post-transplant HU include increased body mass index, reduced eGFR in 24 month after kidney transplantation, cy.

BOS620 INCIDENCE OF AVASCULAR NECROSIS AFTER KIDNEY TRANSPLANTATION DECREASES IN THE MODERN ERA OF IMMUNOSUPPRESSION

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Background: Kidney transplant recipients (KTRs) are at risk of avascular necrosis (AVN) due to chronic kidney disease mineral and bone disorder, steroid use, predisposing comorbidities as diabetes, hypertension, autoimmune disease. AVN is a devastating complication after transplantation impacting quality of life. The knowledge on risk factors and outcome of AVN among KTRs remains scarce.
Methods: We analyzed a total of 765 KTRs from 2005 to 2015 for the development of AVN. Cases of symptomatic AVN were diagnosed by hip X-ray or magnetic resonance imaging. KTRs without AVN served as controls. KTRs with AVN were classified into early and late development of AVN. We evaluated risk factors, kidney allograft outcome and long-term course of AVN with/-out joint replacement. In addition KTRs with joint replacement due to trauma were used for comparison.
Results: 24 of 765 KTRs (3.1%) developed AVN, diagnosed a median of 25 months posttransplantation. The incidence of AVN significantly decreased over the study period. 20 of 24 KTRs (83%) showed AVN of the femoral head, 8 of 24 KTRs (33%) had bilateral AVN; 20 of 24 KTRs (83%) underwent joint replacement. Factors associated with development of AVN included use of cyclosporine compared to tacrolimus ($p < 0.01$). Among KTRs with early AVN, 11 of 12 KTRs (92%) had AVN at allograft side. KTRs with early AVN had lower 25-OH Vitamin D levels at diagnosis ($p = 0.045$), KTRs with late AVN were more likely under statin therapy ($p = 0.039$). No differences were observed between KTRs with AVN and those with trauma with respect to short- and long-term outcomes of joint replacement.
Conclusions: Our results suggest an increased incidence of AVN among KTRs receiving cyclosporine compared to tacrolimus. This finding most explains the decreasing incidence of AVN over the study period due to the replacement of cyclosporine by tacrolimus. Our data raise the hypothesis of an ischemic steal syndrome due to the allograft kidney that impact early AVN at allograft side.

BOS621 INFLAMMATORY AND RELATED BIOMARKERS ARE ASSOCIATED WITH POST-TRANSPLANT DIABETES MELLITUS IN KIDNEY RECIPIENTS

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Background: An inflammatory environment may be associated with hyperglycemia in kidney transplant recipients. Here we investigate the association between a wide range of inflammatory related biomarkers and post- transplant hyperglycemia in kidney transplant patients.
Method: This retrospective analysis comprises 852 patients receiving a kidney transplant at the Norwegian national transplant centre between 2007 and 2012, all having a normal oral glucose tolerance test (OGTT) before transplantation. An additional OGTT was performed 10 weeks post-transplant to examine the association between plasma inflammation related parameters and two-hour plasma glucose by uni- and multivariable linear regression models adjusting for BMI, age, dosage of prednisolone, and concentration of calcineurin inhibitors.
Results: Eight out of 20 biomarkers were significantly associated with 2-h plasma glucose in multivariate analyses with the strongest association with soluble tumor necrosis factor type 1 ($p = 0.003$), pentraxin 3 ($p = 0.027$), macrophage migration inhibitor factor ($p = 0.034$), growth differentiation factor 15 ($p = 0.028$). These associated markers reflect several distinct, but also overlapping pathways including activation of macrophages, granulocytes and endothelial cells. Some of these are also related to extracellular matrix regulation.
Conclusion: These findings suggest a link between inflammation and development of PTDM, and some of these markers may be target for future studies on pathogenesis and treatment of PTDM.

		Univariable regression				Multiple regression			
Biomarker	Mean value	*B*-value	Significance	*R*-square	Conf. interval	*B*-value	Significance	*R*-square	Conf. interval
sTNFR1	1.84	0.696	0.000	0.037	0.454–0.937	0.483	0.003	0.079	0.163–0.803
GDF-15	2.95	0.287	0.000	0.025	0.167–0.407	0.146	0.028	0.073	0.016–0.277
MIF	8.44	0.034	0.021	0.060	0.005–0.063	0.031	0.034	0.072	0.002–0.059
Cat S	24.54	0.0037	0.005	0.010	0.011–0.063	0.024	0.066	0.071	−0.002 to 0.050
Ykl-40	112.84	0.007	0.000	0.050	0.005–0.009	0.005	0.000	0.091	0.003–0.008
EPCR	20.20	0.020	0.022	0.006	0.003–0.037	0.021	0.013	0.100	0.005–0.038
PTX3	4.79	0.088	0.004	0.010	0.027–0.148	0.071	0.027	0.096	0.008–0.135
NGAL	249.93	0.002	0.010	0.008	0.001–0.004	0.002	0.037	0.207	0.000–0.005
Granulysin	3.64	0.092	0.052	0.004	−0.001 to 0.184	−0.009	0.881	0.098	−0.134 to 0.115
IGF1	300.55	−0.001	0.096	0.003	−0.002 to 0.000	0.000	0.506	0.083	−0.001 to 0.001
IGFBP1	117.18	−0.003	0.008	0.009	−0.005 to (−0.001)	−0.003	0.031	0.092	−0.006–(−0.001)
Chemerin	247.41	0.000	0.885	0.000	−0.003 to 0.003				
CXCL16	1.50	0.265	0.413	0.001	−0.370 to 0.900				
Syndecan-1	4.96	0.023	0.249	0.002	−0.016 to 0.061				
GAS6	3.79	−0.020	0.500	0.001	−0.077 to 0.038				
AXL6	10.54	0.021	0.483	0.001	−0.037 to 0.078				
OPN	62.38	0.0001	0.989	0.000	−0.010 to 0.010				
Resistin	29.89	0.006	0.384	0.001	−0.008 to 0.021				
IGFBP3	3.73	−0.081	0.417	0.001	−0.278 to 0.115				
Periostin	242.63	−0.001	0.499	0.001	−0.002 to 0.001				

BOS622 PLASMA TRANS FATTY ACID (TFA) LEVEL-PATIENT AND GRAFT SURVIVAL

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Background: An increased risk of cardiovascular (CV) morbidity and mortality have been reported with high consumption of trans fatty acids (TFAs) in various populations.
Methods/Materials: In this single center cohort study of 1990 Norwegian renal transplant recipients (RTRs), transplanted between 1999 and 2011, we assessed associations between plasma levels of TFAs ten weeks post-transplant and patient and graft survival, using multivariate Cox regression and competing risk analysis as appropriate. Plasma phospholipid fatty acid levels were determined by gas chromatography and quantified as weight percentage of total fatty acids (wt%).
Results: The median TFA level was 0.48 wt% (IQR 0.40–0.56) in 1999 to 2004 and dropped to 0.33 wt% (IQR 0.28–0.39) in 2005 to 2011. During follow-up (median of 6.8 years) the total number of deaths was 406, of which 164 were due to CV disease, and 229 patients returned to dialysis therapy or renal

retransplantation (death censored graft loss). Strong positive crude associations or trends between plasma TFA levels and all-cause mortality (HR 2.78, 95% CI 1.38–5.62), CV mortality (SHR 2.86, 95% CI 0.96–8.52), overall graft loss (HR 2.24, 95% CI 1.23–4.09) and death censored graft loss (SHR 1.65, 95% CI 0.59–4.63) were weaker and statistically insignificant after adjustment for traditional and transplant specific risk factors and transplant era. Patients with high levels of TFAs were clustered together with smokers and malnourished patients, creating a confounder effect (all-cause mortality: adjusted HR 1.23, 95% CI 0.53 – 2.86).
Conclusions: A strong crude inverse association between plasma TFA level and survival, in line with findings from other patient populations, were no longer clinically or statistically significant after adjustment for confounders. Dietary recommendations possibly had a major impact on TFA consumption during the study period and lack of data on temporal changes in TFA levels might have influenced results.

BOS624 SURGICAL OR MEDICAL TREATMENT FOR TERTIARY HYPERPARATHYROIDISM; A SYSTEMATIC REVIEW

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Introduction: A significant portion of patients with chronic kidney disease and secondary hyperparathyroidism (sHPT) remain hyperparathyroid after kidney transplantation, a state known as tertiary hyperparathyroidism (tHPT). Without treatment, tHPT can lead to diminished kidney allograft and patient survival. Parathyroidectomy was commonly performed to treat tHPT until the introduction of the calcimimetic drug cinacalcet. Currently it is unknown which treatment is superior.
Methods: A systematic review was performed and medical literature databases were searched for studies written in English and published after 2003 (cinacalcet was approved in 2004) regarding the treatment of tHPT.
Results: A total of 1669 articles were identified of which 47 were included in the review. After subtotal and total parathyroidectomy initial cure rates were 98.7% and 100%, respectively, however in 7.6% and 4.2% of patients tHPT recurred. After treatment with cinacalcet, 81% of the patients achieved normocalcaemia. Due to side effects, 6.4% of the patients discontinued cinacalcet treatment. Although literature regarding graft function and survival is very limited, however renal graft survival after surgical treatment seems comparable to therapy with cinacalcet.
Conclusion: Surgical treatment for tHPT has higher cure rates than medical treatment. Side effects and complications of both treatment modalities were mild and occurred in a minority of patients. Data regarding clinical endpoints is scarce. This systematic review suggests that (sub)total parathyroidectomy is the preferred treatment for tHPT.

BOS625 RECIPIENT RS1045642 POLYMORPHISM (ABCB1) IS ASSOCIATED WITH OFFICE BLOOD PRESSURE AT ONE-YEAR POST KIDNEY TRANSPLANTATION (KT): A SINGLE CENTER PHARMACOGENETICS COHORT STUDY

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Background: Among adverse events associated with corticosteroids (CS) use after kidney transplantation (KT), reduction of bone mineral density (BMD) and water and salt retention leading to high blood pressure (BP) are the most commonly described. CS are substrates from P-glycoprotein coded by the highly polymorphic *ABCB1* gene. We hypothesized that one of its polymorphism, rs1045642, is associate with BP and BMD parameters at one year post KT.
Methods: Rs1045642 was genotyped using pyro-sequencing in 40 kidney-transplanted recipients. Both dominant (CC vs. CT+TT) and co-dominant (CC vs. CT vs. TT) genetic models were assessed using analysis of variance (ANOVA) from linear regressions to test significant associations between genotypes and BP or bone associated outcomes. Analyses were adjusted for confounding variables such as: age, gender, type of nephropathy, glomerular filtration rate and Cs at one year.
Results: Mean systolic BP (SBP) were 145 mmHg (95% CI = 137–153) for CC, 130.7 mmHg (95% CI = 123.6–137.7) for CT and 129.7 mmHg (95% CI = 114.6–144.8) for TT carriers. Mean diastolic BP (DBP) were 86.5 mmHg (95% CI = 91.7–81.3) for CC, 78.1 mmHg (95% CI = 83–73.3) for CT and 78.7 mmHg (95% CI = 90.2–67.1) for TT carriers. Genotypes were significantly associated with both SBP and DBP measured one year after transplantation, independently of the genetic model used for the analyses and even after adjusting for confounders (adjusted codominant model, SBP: p-value = 0.015, DBP: p-value = 0.038; adjusted dominant model; SBP: p-value = 0.003, DBP: p-value = 0.011). Also, there was a trend in the association of rs1045642 with the BMD evolution at one year after KT.
Conclusion: The CC genotype for rs1045642 is statistically significantly associated with higher blood pressure one year after KT, but not with evolution of bone phenotypes one year post KT. Further investigations are needed to confirm a role for rs1045642 in Cs associated adverse effects.