SHORT ORAL PRESENTATIONS ON POSTERS

SHORT POSTER PRESENTATIONS I: LIVER

PV001 SMALL ANIMAL MODEL OF NORMOTHERMIC EX VIVO LIVER MACHINE PERFUSION FOR LIVER TRANSPLANTATION

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Introduction: Normothermic ex vivo liver machine perfusion (NEVLP) may be used to resuscitate liver grafts otherwise unacceptable for transplantation. Currently employed perfusion systems for liver grafts from large animals or even human livers are too cost-intensive for extensive investigations of possible treatment and conservation protocols. Standardized small animal models of NEVLP are still missing for basic research.
Methods: We developed a rat NEVLP system, which sustains dual perfusion via the hepatic artery and portal vein for up to 6 hours at 37°C with a total priming volume of 50 mL. Moreover, we adapted our perfusion protocol to currently clinically used NEVLP settings. Rat erythrocytes at a hematocrit of 20% serve as oxygen carriers to satisfy the metabolic need during NEVLP. The perfusate includes essential amino acids and taurocholic acid. Epoprostenol is used to prevent vasospasm during dual perfusion. A dialysis circuit connected in parallel helped to maintain electrolyte concentrations as well as the pH physiologic over the perfusion period.
Results: Using this complex perfusion setup, we achieved reduced transaminase release into the perfusate, and sustained liver function during perfusion as measured by total urea and bile production. H&E stains and immunohistology analysis revealed minimal necrosis and improved survival of non-parenchymal liver cells.
Conclusion: In conclusion, our NEVLP system can sustain rat liver grafts at physiological conditions for up to 6 hours. Our system is currently used to develop a variety of protocols to treat pre-damaged organs with subsequent transplantation in order to translate these concepts into clinical application.

PV002 IS THERE A TOO OLD IN LIVER DONORS? AN AGE STRATIFIED ANALYSIS OF ELDERLY LIVER DONORS ABOVE 65

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Introduction: Scarcity of available organs for patients on the liver waiting list has led to an increase in accepting marginal grafts. While it has been established that donor age above 65 years is an independent risk factor for graft loss, further analyses within this cohort are still limited. Aim of this analysis was to investigate the influence of stratified donor age on 1-year outcome after orthotopic liver transplantations (oLT).
Methods: A retrospective analysis including all oLT patients at the University Hospital Münster between 2006 and 2017 was conducted. Eligible patients were stratified for donor age: ≥65–69 vs. ≥70 years of age. Baseline donor and recipient characteristics were compared, and primary endpoint was 1-year patient survival. Secondary endpoints were overall 1-year graft survival, rates of primary non-function (PNF) and frequencies of re-transplantation.
Results: A total of 350 oLT patients were identified, of which 47 (13.4%) received a graft ≥65–69 (66.8 ± 1.5) and 35 a graft ≥70 (74.6 ± 3.9, $p < 0.0001$) years of age. Both groups revealed a comparable recipient age of 55.7 (range 38–71) and 56.1 (range 23–73) years ($p = 0.88$), respectively. Age difference between donor and recipient was 10.4 ± 8.5 (donor ≥65–69) and 18.14 ± 12.38 years (donor ≥70, p = 0.002). Baseline characteristics (indication for oLT, ischemia times, MELD score and donor risk index) were similar. One-year patient survival was 76.6% (≥65–69) and 68.6% (≥ 70, $p = 0.402$). Overall 1-year graft survival was 72.3% (donor ≥65–69) and 65.7% (donor ≥70, $p = 0.509$). Rates of PNF were 14.8% (≥65 to 69) and 8.5% (≥70, $p = 0.387$) and frequencies of re-transplantation were 8.5% (≥65 to 69) and 14.2% (≥70, $p = 0.237$).
Conclusion: A slightly higher but not significant increase in overall graft loss, lower patient survival and higher frequencies of re-transplantation was found in recipients who received a graft from a donor above the age of 70 compared to those between 65 and 69. While both groups had acceptable survival rates, these results demonstrate that within the high risk group of elderly donors, donor age above 70 years is associated with an increased risk for inferior outcome within the first year after oLT.

PV003 LONG-TERM OUTCOME OF DIFFERENT REPERFUSION SEQUENCES IN HUMAN LIVER TRANSPLANTATION

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Introduction: Despite the fact that most liver transplant centers perform reperfusion via the portal vein in human liver transplantation for historical reason, there is so far no conclusive evidence how to reperfuse livers best. This retrospective study analyses long-term outcome of different reperfusion sequences (primary portal venous reperfusion (PV) vs. primary arterial reperfusion (A) vs. simultaneous reperfusion (Sim)).
Methods: All patients undergoing liver transplantation in 2006/2007 were evaluated for analysis. Only patients who received a primary, whole organ liver graft were included. Re-transplantations and combined liver-pancreas transplantations were excluded, resulting in 61 patients qualifying for analysis. Primary portal venous reperfusion was performed in 25, primary arterial reperfusion in 22 and simultaneous reperfusion in 14 recipients.
Results: After 12 years, 21 patients were still alive (35% of the study population). Mean age at time of transplantation was 55 years. Despite the fact that patients in the simultaneous reperfusion group were the oldest (59 y vs. 55 y (A) vs. 50 y (PV), p = 0.01), overall mortality rates were the lowest in this group (50% vs. 68% (A) vs. 72% (PV). Mean overall survival was 5.87 years (A), 5.03 years (PV) and 8 years (Sim, n.s.) with a graft survival of 5.5 years (A), 3.7 years (PV) and 8 years (Sim), p = 0.04. Re-Transplantation was performed in 9 patients (12.5%). Interestingly, none of the patients of the simultaneous reperfusion group required re-transplantation while the rate was 24% in the PV-group.
Conclusion: Although simultaneously reperfused recipients were the oldest, this study population showed superior results in terms of overall and graft survival. Additionally, there was no need for re-transplantation when compared to the PV and A reperfusion groups. Further multicentric RCTs with larger study populations are needed to support this observation.

PV005 PORCINE DERMAL COLLAGEN FOR ABDOMINAL CLOSURE AFTER PEDIATRIC LIVER TRANSPLANTATION

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Introduction: Primary abdominal wall closure (PC) after pediatric liver transplantation (pLT) can become challenging based on graft to recipient size mismatch and pre-existing abdominal wall defects due to previous surgeries. Herein we describe our experiences with the use of porcine dermal collagen graft (PDCG) as acellular graft for abdominal wall closure after pLT in patients <2 years.
Methods: Retrospective analysis of patients younger than 2 years undergoing pLT between 01/2011 and 12/2014. Patients were divided into PC- and PDCG groups. GTBW ratio was calculated using the formula 706.2x√[donor body surface area (m^2) + 2.4]/1000/recipient weight (kg)). Primary endpoints were post-operative abdominal wall infections. Secondary endpoints included 1- and 5-year patient and graft survival (assessed by Kaplan Meier estimates) and development of abdominal wall hernia (T-Test).
Results: 16 out of 21 patients (76.2%) received a PDCG with a median of 22.8 (SD ± 11.0) days after pLT. Children receiving a PDGC did not have significantly more abdominal surgeries before pLT (50.0%) when compared to the control (60.0%, p = ns). There was no difference in graft types within the

two groups. A median of 3.4 (SD ± 1.9) surgeries after pLT took place prior to PDGC implantation and a median of 2.1 (SD ± 2.2) surgeries before final abdominal wall closure in the PC group (p = ns). One PDGC patch had to be removed due to infection, no further abdominal wall infections occurred in the whole cohort. Thromboembolic complications (hepatic artery and portal vein thrombosis) occurred more frequent prior to definite closure in PDCG group when compared to PC group (37.5% in PDCG group and 0.0% in PC group). Median GTBW ratio was 4.0% (SD ± 1.2) in PDCG group compared to 3.8% (SD ± 0.6; p = ns) in PC group. 2 children died before definite abdominal wall closure. For the remaining patients, 1-year and 5-year patient survival was 100% and 100% in PDCG group and 100% and 80% in PC group, respectively (p = ns). Abdominal wall hernias were observed in two patients of the PDCG group (12.5%) and none in the PC group (0.0%; p = ns).
Conclusion: PDGC can be safely used for abdominal wall closure after liver transplantation in children <2 years of age.

PV006 THE INFLUENCE OF BRIDGING PROCEDURES ON SURVIVAL AFTER LIVER TRANSPLANTATION FOR HCC

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Introduction: Tumor recurrence is the leading cause of death after liver transplantation (LT) for patients with hepatocellular carcinoma (HCC). We evaluated the influence of bridging procedures on survival after liver transplantation for HCC.
Methods: We extracted data of HCC patients who underwent liver transplantation (LT) between 1996 and 2017 from our prospectively maintained tumor register. Patients who died within three months after LT were excluded.

We analyzed the tumor load, pre transplant α-Fetoprotein (AFP) (ng/ml) level, Child Stage, use of bridging therapy and type of LT. Survival rates were calculated with the Kaplan-Meier procedure and significance testing was performed with the log-rank test. Starting point for survival calculation was the date of LT. End point for observed and tumor-related survival was dead of any cause and dead of hepatocellular carcinoma, respectively.
Results: 76 out of 163 patients hat no bridging therapy. The other 87 patients (54%) had – multiple or combined if indicated – transarterial chemo embolization, radio frequency ablation, yttrium ^{90} radio embolization. In 20 cases this resulted in a complete regression of the tumor before LT. Median follow-up-time was 55 months (Range 4–264). Median observed survival time was 106 months. By now, 71 patients died, 37 of them of recurrence of tumor, 34 of other causes.

Observed 5- and 10 year survival rates with bridging were 67 ± 5% and 47 ± 7%, without bridging 56 ± 5% and 46 ± 7%, respectively. In contrast, tumor-related 10-year survival rates showed a statistically significant difference (81 ± 5% versus 59 ± 7%). Bridging, type of LT, number and diameter of lesions, Milan score and AFP level were included in a COX-procedure. Here bridging, number of lesions, and α-Fetoprotein level showed an independent statistically significant influence on tumor related survival.
Conclusion: Bridging therapy is able to reduce tumor recurrence and death of tumor in transplanted HCC patients.

PV009 GENDER DISCRIMINATION VIA MELD-BASED LIVER ALLOCATION IN GERMANY

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Introduction: MELD was implemented to guarantee urgency-based and fair organ allocation. Nonetheless men are outnumbering women as liver transplant recipients. The aim of this study was to analyze gender disparities in liver transplantation particularly with regard to organ allocation in a nationwide cohort.
Methods: All liver transplantations – excluding pediatric recipients, combined organ transplantation and living donors – from 2005 to 2015 in Germany were assessed retrospectively using the data record of Eurotransplant.
Results: 9832 liver transplantations fulfilled all criteria in the investigated period. Nearly two thirds (6466, 65.8%) of all recipients were male. This percentage was even higher in patients allocated by regular allocation without high urgency status (male 68.7%).

Latest laboratory MELD score as well as MatchMELD score were higher in women compared to male recipients (23 vs. 18, p < 0.001 and 28 vs. 26, <0.001, respectively). Men on the other side were more likely to have an exceptional status compared to women (30.9% vs. 23.4%, p < 0.001) as 80% of all transplantations for hepatocellular carcinoma occurred in men. In contrast, common indications for women are not considered for standard exceptions (e.g. PBC – 77% females). Besides this discrimination in indications laboratory values of the MELD score differed by gender. Although women showed better serum creatinine values (1.38 mg/dl vs. 1.6 mg/dl, p < 0.001) eGFR was significantly lower (65.9 vs. 69.2, p < 0.001). Despite being sicker, women do not generate high MELD scores due to lower muscle weight. Therefore, their Bilirubin (11.02 vs. 8.77, p < 0.001) and INR (2.02 vs. 1.72, p < 0.001) had to achieve higher values before getting organ offers. The mean difference in creatinine values corresponded to approximately two points in the labMELD score.
Conclusion: There is a significant gender inequity in liver transplantation recipients. Probably this can be partially explained by varying incidences of liver diseases, but MELD based allocation seems to aggravate the injustice. A critical analysis whether access to liver transplantation is equal for all genders is needed.

PV010 EXCELLENT OUTCOME QUALITY IS NOT DEPENDENT ON A HIGH CASELOAD IN LIVER TRANSPLANTATION

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Introduction: The current dogma is that case volume correlates with patients' outcome. Furthermore, interdisciplinary and interprofessional concepts are thought to add to quality in patient care. However, the overall benefit of such concepts for survival after liver transplantation (LT) is unknown. Therefore, the effect of systematic structured interdisciplinary and interprofessional collaboration was evaluated in a low volume center prospectively.
Methods: Our LT program was re-organized and re-structured in 2016 including a center-embedded interdisciplinary and interprofessional team concept with new clinical standards for the peri-, intraoperative and follow-up management of patients. In parallel, routine pre-transplant histopathological evaluation of donor organs was established. Ever since outcome quality after LT was documented in a prospective, database and compared with high volume centers. Adult patients who underwent first LT between November 2016 and May 2019 were investigated, and outcome data were analyzed. Kaplan-Meier method was used for long-term patient and graft survival.
Results: 94 liver transplantations (73 male patients, median age of 56.4 years [19 to 74 years]) were performed with a 1-year patient and graft survival of 95.6% and 92.0%, respectively. The median ICU stay was 2 days [1–114 days] and the median hospital stay was 20 days [9–147 days]. Hospital readmissions were necessary within the first 30 days and 1 year after discharge in 8% and 16% of cases, respectively.
Conclusion: Clearly defined standards developed within an interdisciplinary and interprofessional team concept result in best possible outcome quality of treatment after LT independent of caseload.

SHORT POSTER PRESENTATIONS II: BASIC SCIENCE

PV011 ORAL PRECONDITIONING OF DONORS AFTER BRAIN DEATH WITH CALCINEURIN INHIBITORS VS. INHIBITORS OF MAMMALIAN TARGET FOR RAPAMYCIN IN PIG KIDNEY TRANSPLANTATION

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Introduction: Data regarding donor preconditioning with calcineurin inhibitors (CNIs) and/or inhibitors of mammalian target for Rapamycin (mTORIs) are limited. The aim of this project is to investigate the effects of (oral) donor preconditioning with a CNI (Cyclosporine A) versus an mTORi (Everolimus) compared to the conventional administration of steroid in the setting of DBD in porcine renal transplantation.
Methods: After the induction of brain death, German landrace donor pigs (33.2 ± 3.9 kg) were randomly preconditioned with either Cyclosporine (n = 9) or Everolimus (n = 9) administered via nasogastric tube. Control donors received intravenous (i.v.) Methylprednisolone (n = 8). Kidneys were procured, cold-stored in HTK solution at 4 °C and transplanted in nephrectomized recipients after a mean cold ischemia time of 19.32 ± 2.92 (SD) hrs (range: 15.33–25.83). No immunosuppression was performed to avoid confounding

bias. Blood samples were obtained at 4 hours postreperfusion and daily until postoperative day (POD) 5 for complete blood count, blood urea nitrogen (BUN), creatinine (Cr), and electrolytes. Graft protocol biopsies were performed 4 hours after reperfusion.
Results: There was no difference in the hemodynamic parameters, hemoglobin/hematocrit and electrolytes between the groups. Serum BUN peaked on POD1 in all groups but trended to remain higher after donor preconditioning with Everolimus. Serum Cr also peaked on POD1 but was significantly higher after donor preconditioning with Cyclosporine on POD 1 ($p = 0.017$) and at the conclusion of the study on POD 5 ($p = 0.009$). There was no difference between serum Cr after donor preconditioning with Everolimus compared to steroids. Histological assessment revealed no significant differences between the groups.
Conclusion: Donor oral preconditioning with Everolimus (but not Cyclosporine) resulted in similar post-transplant serum Cr values compared to the conventional donor preconditioning with i.v. steroids after porcine kidney transplantation. The histological Tissue damages were the same in the 3 groups, showing no advantage in the conventional preconditioning group.

PV012 BACK SIGNALING OF HLA CLASS I MOLECULES AND T/NK CELL RECEPTOR LIGANDS IN RENAL EPITHELIAL CELLS CONTRIBUTES TO THE REJECTION-SPECIFIC MICROENVIRONMENT

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Introduction: During the last years, diverse harming mechanisms of donor-specific antibodies (DSA) to endothelial cells have been studied accompanied by an emerging evidence of T/NK cell involvement in antibody-mediated rejection (ABMR).
Methods: Proximal tubular epithelial cells (PTEC) were stimulated via HLA class I and T/NK cell receptor ligands, CD155 and CD166, which were selected based on their potential signal-transducing capacities to mediate back signaling after T/NK cell encounter or donor-specific antibody ligation. Cytokines and chemokines were quantified using Bio-Plex assays. The PTEC cytokine response was compared to the cytokine/chemokine microenvironment of 44 kidney transplant biopsies, classified as unsuspicious, TCMR, borderline or ABMR rejection according to the BANFF classification.
Results: Upon stimulation with anti-HLA and anti-CD166 mab, PTEC secreted IL-6, CXCL1, 8, 10, CCL2 and sICAM-1 (all $p < 0.05$). Clinically approved immunosuppressive drugs and other signal inhibitors were unable to block this back signaling and, hence, revealed a complex regulatory network upon triggering HLA class I and T/NK cell receptor ligands. PTEC cytokine/chemokine signature was reflected in rejection-specific microenvironment, especially ABMR, in renal allograft biopsies, guided by significantly higher levels of chemokines (CXCL9, CXCl10 and CCL5 and CCL2 all $p < 0.05$).
Conclusion: Our observations indicate an impact of PTEC back signaling to antibody-mediated rejection via chemokine release and may contribute to a better understanding of the pathomechanisms involved in kidney allograft rejection.

PV015 CRYOPRESERVED AMNIOTIC MEMBRANE MAINTAINS ITS REGENERATIVE POTENTIAL AFTER DOUBLE FREEZE-THAWING CYCLES

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Introduction: Amniotic membrane (AM) is widely used in the field of ophthalmology due to its unique anatomical structure and tissue composition. Highly efficient clinical approaches for the treatment of corneal, limbal and conjunctiva pathologies utilizing AM were developed and introduced worldwide. Cryopreservation is a necessary step required in the manufacturing chain between retrieval of AM and application in a patient. In this study, the regenerative potential of human amniotic membrane after cryopreservation was evaluated.
Methods: AM was prepared under sterile conditions and frozen without cryoprotectants at −80°C. Native non-cryopreserved AM served as a control. The strategy for AM cryopreservation included one or two freezing and thawing cycles. Cytokine and growth factor profiles as well as morphology and mechanical properties of AM were compared before and after one and two cycles of cryopreservation. Levels of EGF, HGF, TGF-β1, bFGF, Laminin and Hyaluronic acid were measured by ELISA. Surface structure of the membrane was analyzed by scanning electron microscopy (SEM). Morphology was evaluated by histological analyses after Hematoxylin Eosin (HE) staining. Additionally, biomechanical characteristics, such as the modulus of elasticity (Young's modulus) and the tensile strength, were also investigated.
Results: EGF, HGF, TGF-β1, bFGF, Laminin and Hyaluronic acid were detected in all studied samples. No significant differences were detected in the levels of those cytokines before and after cryopreservation. SEM analysis showed minor structural alterations of double cryopreserved samples. Analysis of HE stained AM showed minor changes between native and frozen membranes, such as few areas with desquamated epithelium which was caused by repeating freezing and thawing cycles. Mechanical tests did not reveal relevant changes between frozen and non-frozen samples.
Conclusion: Multiple cryopreservation steps are an essential part of manufacturing of human amniotic membranes to ensure a ready-to-use product availability. This study demonstrated that the cryopreservation does not impair the regenerative potential of AM required to support its therapeutic efficacy.

PV017 HEPATOCYTE TRANSPLANTATION AFTER MAJOR LIVER RESECTION – PRELIMINARY RESULTS OF A PORCINE LARGE ANIMAL STUDY

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Introduction: Hepatocyte transplantation (HTx) is of large potential as treatment modality for various liver diseases and represents an additional therapeutic option to liver transplantation in the context of organ shortage. We developed a porcine animal model of hepatocyte transplantation after major liver resection in order to investigate the safety and feasibility of this novel approach.
Methods: Donor livers were procured according to protocols applied in humans (i.e. arterial perfusion with HTK-solution), thereafter porcine hepatocytes were isolated using a 3-step-collagenase perfusion technique. Two protocols for HTx were tested: In the first group, six pigs received major liver resection to induce liver function impairment followed by HTx via an exteriorized portal venous catheter directly after surgery. In the second group, HTx was performed three days after major liver resection in five animals.
Results: A mean volume of 136.7 ml and 134.6 ml with 4.09×10^8 and 3.81×10^8 viable hepatocytes were infused in both groups, respectively. HTx was performed pressure controlled with tolerated increase of portal venous pressure up to 25 mmHg and consequently temporary reduction/stoppage of infusion. Portal venous pressure was 19.2 mmHg and 17.8 mmHg before HTx and increased to 25.0 mmHg and 23.6 mmHg, respectively, at the end of cell infusion. All animals remained stable concerning vital parameters during HTx. After hepatocyte transplantation animals of both groups recovered quickly with recurrence to base line for coagulation factors and ammonia on day 15 and 4 after transplantation.
Conclusion: Pressure controlled hepatocyte transplantation immediately after major liver resection as well as three days after surgery was safe and well tolerated in a preclinical large animal model.

PV018 ACUTE ANTIBODY MEDIATED REJECTION (AMR) WITH DETECTION OF ANGIOTENSIN II TYPE 1 RECEPTOR ANTIBODIES (AT1-RA) AFTER PEDIATRIC LIVER TRANSPLANTATION

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Introduction: AMR remains an uncommon finding after liver transplantation, but can cause acute and chronic graft dysfunction. Besides donor specific HLA antibodies, also non-HLA antibodies (e.g. AT1-RA) are gaining importance in this setting.
Methods: Case report.
Results: We report of a 2 year old boy, who was transplanted for the first time at the age of 2 months because of acute neonatal liver failure. The reason was never detected. The first transplant was performed by ABO-compatible living

liver donation from the mother. The course was complicated by repeated rejections resulting in chronic biliary problems and secondary sclerosing cholangitis. The child was re-transplanted at the age of 2 years with a whole liver graft from a deceased donor. The postoperative course was without complications and the boy could be dismissed after three weeks. 6 weeks later he was re-admitted with severely rising liver enzymes and pruritus. The first biopsy demonstrated acute cellular rejection (RAI 8) and a high steroid pulse therapy was initiated. Despite this treatment liver enzymes increased continuously and liver function rapidly deteriorated. A re-biopsy revealed severe lobular hepatitis with disseminated liver cell necrosis being suggestive of fulminant viral hepatitis. Due to increasing signs of liver failure the child was listed for high urgency liver transplantation and transplanted by a living liver donation from the father because no graft from a deceased donor was available. In the explanted liver massive liver cell necrosis as well as signs of acute cellular rejection (RAI 6) were detected. Furthermore a chronic vascular rejection was diagnosed. In the following extended immunologic work up we found pre-existent low titers of AT1-RA already before the primary transplantation with a significant increase of titers before re-transplantation. Because of this finding we initiated Candesartan treatment and our patient shows no new signs of rejection or organ dysfunction 12 weeks after re-re-transplantation.
Conclusion: Besides acute cellular rejection also AMR with non-HLA antibodies can cause fulminant graft failure and should be considered as potential reason for acute graft failure.

PV019 HEART-ASSOCIATED CYTOKINE AND ENDOTHELIAL PATTERNS DOMINATE THE ISCHEMIA/REPERFUSION RESPONSE IN RECIPIENTS OF COMBINED HEART/LUNG TRANSPLANTATION IN COMPARISON TO LUNG TRANSPLANTATION

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Introduction: Organ-specific differences are discussed for ischemia/reperfusion injury (IRI) in cardiothoracic transplantation (Tx) but rarely compared directly in a clinical setting. Therefore, we compared a cohort of combined heart/lung transplants (HLTx) with cohorts of isolated heart (HTx) or lung transplantations (LTx), respectively, with respect to cytokines and endothelial markers in recipient blood and perfusates. Despite the evident clinical differences, our aim was to determine whether the microenvironment of HLTx patients would be rather related to HTx or LTx patients.
Methods: Blood plasma pre Tx and post Tx at T0, T24 and 3 weeks as well as perfusion solutions of 5 HLTx, 24 HTx and 21 LTx patients were analysed for cytokines and soluble endothelial markers using multiplex assays.
Results: Early after transplantation at T0 and T24, HLTx and HTx recipients displayed significantly higher plasma levels of IL-6, CXCL8/IL-8, Ang-2, IGFBP-1, PAI-1 compared to LTx recipients that returned to baseline after three weeks. Identical kinetics with minimal changes were detected in the three groups for TNF, HB-EGF, EGF, PLGF, sFasL, TGF-α. Unsupervised cluster and principal component analyses clearly grouped HLTx and HTx patients together, separating LTx recipients apart with IGFBP-1, Ang-2, and PAI-1 as lead parameters (all $p < 0.01$). In contrast, HLTx perfusates were grouped together with LTx and not HTx indicating that this compartment is dominated by the lung rather than the heart.
Conclusion: A direct comparison of combined heart/lung with isolated heart or lung transplantation revealed that the systemic IRI response of HLTx recipients is, perhaps counterintuitively, dominated by heart-associated endothelial markers like IGFBP-1, Ang-2, and PAI-1 which groups them together with HTx patients. The difference between recipient blood and perfusates strongly suggests that the ischemia response is dominated by lung whereas the systemic reperfusion response is guided by heart. These results underline the organ-specific impact on IRI with distinct heart- vs lung-associated signatures.

PV020 CLUSTERING ALGORITHMS FOR EX VIVO PERFUSED KIDNEYS IN NORMOTHERMIC MACHINE PERFUSION

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Introduction: Normothermic ex vivo kidney perfusion provides functionality assessment of marginal organs and the opportunity for reconditioning of the graft. Currently the lack of organ donors in Germany is aggravated by the increasing age of donors. The kidney graft is perfused at normothermic temperature with an oxygenated blood-based solution. Our system collects data of kidney temperature, perfusion pressure and blood flow. Additionally it provides regulation opportunities. After perfusion unsupervised learning methods like cluster analyses offer the possibility to find groups (acceptable/not acceptable) in histological data based on similarities.
Methods: This study contains 19 kidneys from domestic pigs in a standard setup for organ retrieval, priming and reperfusion. To induce a marginalisation of organ a prolonged warm ischemia (>45 min) in situ was set in subgroup of organs (47% of kidneys). After retrieval the organs were grouped, the cold storage differed from 1–11 hours. After cold storage every organ was perfused in a 4-hour ex vivo perfusion with autologous blood at 38 °C. Perfusion pressure was regulated to 100 mmHg. Regularly blood gas analyses were taken with radiometer ABL80. After perfusion three areas of kidneys were histological examined with Masson-Goldner-Trichrome reaction and Periodic-acid-Schiff (PAS) reaction.
Results: The results were blinded and partitioned in two groups (acceptable/not acceptable) under use of automated histological and Fuzzy c-means clustering methods. The grouping shows that 44.5% of previously marginal kidneys and 100% of previously acceptable organs are acceptable for transplantation.
Conclusion: Based on histological data, this examination shows that marginal organs at a high percentage are still acceptable for transplantation. An automated classification with algorithms of machine learning based on haemodynamic and blood gas parameters to replace time-consuming histological evaluation is in progress. Thus, previously unused organs might be provided for transplantation. Furthermore, the success rate of marginal kidney transplantation could be increased.

SHORT POSTER PRESENTATIONS III: KIDNEY

PV021 POSTTRANSPLANT TUBERCULOSIS IN EUROPE– A TB NET STUDY

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Introduction: Evidence on tuberculosis incidence and management of risk of tuberculosis after solid organ transplant in Europe is scarce.
Methods: The effect of screening with TST/IGRA on tuberculosis incidence rates after solid organ transplant is assessed in successive solid organ transplant patients from 2007 to 2012 in transplant centres across Europe in a multivariate survival analysis, accounting for competing risk of death and clustering by transplant centre. Regional differences of transplant centers incidence rates are assessed in a fixed effects meta-analysis on standardized incidence ratios of posttransplant tuberculosis.
Results: Of 6534 patients (72% kidney, 17% liver, 11% heart/lung) in 15 transplant centers from 8 countries, 37 developed tuberculosis during 33261 person years (pys). 31% were screened with TST/IGRA and 110/236 (46%) of those positive were offered chemoprevention.

Tuberculosis incidence rates after solid organ transplant was 111/100.000 pys (95%CI 81–154 pys), highest in the first two years after solid organ transplant (321/100.000 pys). There was no evidence of reduced tuberculosis incidence rates after screening (HR 0.6, 95%CI 0.3–1.4) adjusting for sex, age, immigration, ethnicity, country/type of solid organ transplant, previous TB, alcohol, diabetes and smoking. However, if screened positive but not offered chemoprevention patients had higher tuberculosis incidence rates than if not screened (HR 2.9, 95%CI 1.6–5.3).

The meta-analysis yielded high standardized incidence ratios in southern Europe (Spain/Portugal, pooled SIR 14, 95%CI 6.5–21.8) compared to central Europe (Austria, Czech Republic, Germany, Netherlands, Serbia, UK, pooled standardized incidence ratios 3.7, 95%CI 0.5–6.9), with the highest crude tuberculosis incidence rate in a liver-transplant centre in Portugal (729/100.000 pys, 95%CI 414–1284).
Conclusion: We found highly variable posttransplant tuberculosis incidence rates. While tuberculosis is a rare event in central Europe, IGRA/TST screening and subsequent chemoprevention of solid organ transplant patients in particular in southern Europe should be harmonized.

PV022 SURGICAL OUTCOMES OF RENAL TRANSPLANT RECIPIENTS AFTER ABDOMINAL SURGERY NOT CONNECTED WITH TRANSPLANTATION. A RETROSPECTIVE CASE-CONTROL STUDY

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Introduction: Due to the increasing number of patients after kidney transplantation, elective and emergency surgery of transplanted patients is becoming a relevant challenge in clinical routine. The current data on complication rate of patients after kidney transplantation, which must undergo another elective or emergency abdominal surgery, are inhomogeneous. Therefore, the aim of our study was to evaluate the outcome of renal transplant patients undergoing abdominal and abdominal wall surgery.
Methods: We performed an observational study of patients after kidney transplantation undergoing graft-unrelated abdominal surgery between 2005 and 2015. We randomly created a non-transplanted control for a case-matched controlled analysis. Primary endpoint was the comparison of complication rate. Secondary, a risk analysis of all patients was performed and differences in mortality, length of hospital stay and reoperation rates were calculated.
Results: Overall 101 kidney transplanted patients were eligible for inclusion. 20 (19.8%) died after graft-unrelated surgery and 60 (59.4%) suffered from postoperative complications. Case-matched analysis could be performed for 84 out of these 101 patients. We found no significant difference in morbidity rate (58.3% vs. 45.2%, $p = 0.090$). Transplanted patients had, however, a significantly higher mortality (19% vs. 2.4%, $p = 0.001$), a longer hospital stay (28.2 vs. 16.9 days, $p = 0.02$) and a higher rate of re-operations (38.1% vs. 20.2%, $p = 0.017$).
Conclusion: Patients after renal transplantation undergoing graft-unrelated abdominal surgery have a significantly increased mortality risk, are more frequently re-operated and have to stay significantly longer in hospital than non-transplanted patients.

PV023 TRANSPLANTATION OF AN HCV-INFECTED KIDNEY TO AN UNINFECTED PATIENT

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Introduction: Renal transplantation has proven to be the optimal therapeutic option for end-stage renal disease (ESRD), increasing expectancy and quality of life. However, the organ shortage especially in blood group 0 needs approaches to expand the donor pool. In the past, many organs from young, HCV-infected donors were not used due to the risk of HCV-transmission. Direct antiviral agents offer a possibility to use HCV-positive organs for transplantation.
Methods: We report our first transplantation of an HCV-positive kidney. A serum HCV RNA level of 106 copies/ml of HCV genotype 1b was detected in the blood of the donor. The recipient, a 49-year-old female patient, suffered from ESRD caused by an atypical hemolytic uremic syndrome. A long waiting time was expected because she had blood group 0.
Results: In December she received an AB0-compatible kidney transplant from an HCV-RNA positive, 33-year-old donor. Hemodialysis and infusion of Eculizumab were performed prior to the surgery. The surgery was carried out without complications. The initial immunosuppressive therapy consisted of prednisolone, mycophenolate sodium, and tacrolimus. Furthermore, an inductive therapy with basiliximab was given on day 0 and day 4. The graft started working on postoperative day four, and the serum creatinine decreased to 1.33 mg/dl on the discharge day.

Due to the initially unknown genotype of the HCV, a pangenotypic HCV prophylaxis with glecaprevir and pibrentasvir was given immediately post-surgery and carried on during the post-transplant time for eight weeks. The patient developed anti-HCV antibodies within six days after transplantation. Frequent HCV-PCRs over six months showed negative results.
Conclusion: We conclude that kidneys from HCV viremic donors can be transplanted with precaution to selected patients to reduce waiting time and to increase survival time. The combination of glecaprevir and pibrentasvir offers a safe HCV prophylaxis without the need of adaptions due to changes of the renal function or genotype detection. Further studies are needed to find the optimal time for the beginning with direct antiviral agents for HCV (D+/R-) transplantations.

PV024 LECTIN STAININGS IDENTIFY GLYCOCALYX INJURY IN RENAL ALLOGRAFTS WITH THROMBOTIC MICROANGIOPATHY (TMA)

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Introduction: TMA is a rare severe disease defined as microvascular endothelial injury, thrombosis, thrombocytopenia and microangiopathic hemolytic anemia, affecting both native and transplanted kidneys. Antibody-mediated rejection (ABMR) and TMA share morphological similarities.
Methods: Sixty accepted morphological criteria for TMA were analyzed in archival routine paraffin sections of 227 grafts (26% from genetically verified aHUS patients) diagnosed with TMA. Ultrastructural and immunohistochemical analyses were done, including visualization of cell surface glycosylation by lectin staining. ABMR samples, normal tissue from tumor nephrectomies and normal control KTx biopsies (normal kidney function) served as controls. All results were correlated with clinical data obtained from the participating 14 nephrology centres.
Results: Patients' (female 37%) age range was 4–76 years. Most grafts (53%) had rejection (cellular 7%, ABMR 34%, mixed 12%). Thrombi were identified in 71% of TMA cases (glomerular 41%, arteriolar 40%, arteries 25%). Most useful histological TMA criteria apart from thrombi were fragmented red blood cells (glomerular 65%, arterioles/arteries 67%), fibrillar appearance of mesangium (66%), endothelial swelling (glomeruli 68%, arterioles 67%), thickened capillary walls (66%), collapse of capillary tuft (92%) and arterial intimal mucoid edema (arteries 78%, arterioles 47%). Morphology (besides thrombi), immunohistochemistry (CD34, thrombomodulin, heparanase-2, C3d, C4d) and ultrastructure could not uncover differences between ABMR with TMA and pure ABMR. Staining with lectins *Sambucus nigra* (SNA; recognizing α2,6-linked sialylation), *Peanut* (PNA; Gal β1->3 GalNAc)l), *Maackia amurensis* (MAL II; α2,6-linked sialylation) and *Erythrina cristagalli agglutinin(ECL;* Gal β1–>4GlcNAc) identified differences in glomerular (SNA, PNA) and peritubular capillaries (SNA, PNA, ECL), podocytes (SNA, PNA), arteries (SNA) and tubuli (SNA) between biopsies revealing ABMR with TMA compared to pure ABMR and controls.
Conclusion: Here, we provide first evidence that analyses of cell surface glycocalyx might be helpful in differential diagnosis in renal grafts and might discover specific injury mechanisms in TMA.

PV026 GRAFT-DERIVED CELL-FREE DNA (GCFDNA) AS A MARKER OF REJECTION AND GRAFT INJURY IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Because traditional methods to assess transplant organ damage are imprecise or invasive, new biomarkers for noninvasive monitoring of graft integrity are needed to personalize immunosuppression.
Methods: In a prospective observational trial, GcfDNA was evaluated in over 1,300 samples at prespecified visits in 189 kidney transplant (KTx) patients over one year post KTx. GcfDNA results were compared between patients with

and without positive biopsies including rejection, borderline rejection, acute tubular necrosis (ATN), interstitial fibrosis/tubular atrophy (IF/TA).
Results: In patients (N = 15) with samples (n = 22) drawn during biopsy-proven acute rejection (BPR), median GcfDNA(cp/mL) was 3.3-fold and median GcfDNA(%) 2.0-fold higher (82 cp/mL; 0.57%, respectively) than the medians observed in samples ("Stable Group": N = 83, n = 408) without any clinical suspected graft injury (25 cp/mL; 0.29%). Results from ATN patients (N = 29, n = 31) were not significantly different from those with BPR. Median values in IF/TA (N = 24, n = 30) were 1.5-fold for GcfDNA(%) and 1.4-fold higher for absolute amount(cp/mL) compared with the Stable Group, but significantly lower than BPR ($p < 0.03$). GcfDNA identified unnecessary biopsies in 6 of 7 patients with negative pathology which were triggered by a rise in plasma creatinine. Diagnostic accuracy was superior for GcfDNA(cp/mL) (AUC = 0.83) compared to GcfDNA(%) (AUC = 0.73). Plasma creatinine showed a low correlation (r = 0.37) with GcfDNA(cp/mL). In a selected subgroup (N = 24) without clinically suspected damage but a change of tacrolimus concentration > 60%, in samples at > 3 consecutive visits, there was a significantly higher rate of elevated GcfDNA(cp/mL) results in samples with lower tacrolimus levels (<8 μg/L) than in higher tacrolimus samples ($p = 0.0036$).
Conclusion: The data show that GcfDNA can detect inadequate immunosuppression resulting in subclinical graft damage. Absolute quantification of GcfDNA(cp/mL) has the advantage of not being influenced by a change of total recipient cfDNA. However, consideration of both, absolute quantification (cp/mL) and GcfDNA fraction together, provides the most comprehensive diagnostic information when assessing allograft injury post KTx
Acknowledgement: This study was funded by the BMBF (PTJ -KMU-innovativ-13: FKZ 031A584A+B).

PV027 ENDOTHELIAL PROGENITOR CELLS IN KIDNEY TRANSPLANTED WOMEN AND IN THEIR OFFSPRINGS

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Introduction: Due to the continuous progress in transplant medicine the long-term survival of transplant patients has substantially improved enabling patients to fulfill their wish for a child. However, there is a higher risk for cardiovascular events as well as for the development of hypertensive disorders in pregnancy, e.g. preeclampsia partly due to the lifelong necessity of immunosuppression. A diminished number of endothelial progenitor cells which play an important role in the repair of endothelial damage and angiogenesis is associated with an increased cardiovascular risk. Further a decreased number and function of these cells is found in maternal and cord blood in preeclampsia. The aim of our study was to evaluate if kidney transplantation affects number and function of different populations of endothelial progenitor cells in women after kidney transplantation and in pregnancy.
Methods: 19 healthy and 20 kidney transplanted women were recruited. The ratio of angiogenic and non-angiogenic circulating progenitor cells was determined by multicolor flow cytometry. Sera of the aforementioned patients and of six umbilical cords of kidney transplanted mothers' offsprings were collected. Endothelial colony forming cells (ECFCs), a proliferative subgroup of endothelial progenitor cells, were incubated with pooled sera and then their functional integrity was analyzed in comparison to healthy controls' sera using in vitro models.
Results: The ratio of angiogenic and non-angiogenic circulating progenitor cells was adversely changed in premenopausal kidney transplanted women ($p = 0.04$) compared to age-matched healthy controls. Sera of transplanted women as well as sera from umbilical cord of transplant patients' offsprings lead to a significant impairment of ECFC proliferation, migration and angiogenesis ability (all $p < 0.001$).
Conclusion: Endothelial progenitor cell functionality is impaired in women after kidney transplantation and immunosuppression. We further suspect an impact on the fetal vascular system which may have long-term effects on offsprings' vascular health.
Acknowledgement: This project was supported by the German Ministry of Research and Education (Reference Number 01EO1302).

PV028 MOLECULAR DIAGNOSIS OF KIDNEY TRANSPLANT FAILURE BY THE URINE

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Introduction: Life threatening organ failure requires urgent organ transplantation. However, shortage of organs and death on the waiting-list is a sad reality. Thus, transplantation is increasingly performed under extended criteria and an exceptional responsibility has developed in assessing postmortal organs consented for retrieval. Rare donor diseases are extremely difficult to assess, particularly since medical information of the donor is often incomplete and time for allocation is restricted. Therefore, such situations are always challenging.
Methods: Histological studies, cell culture of donor human Urinary Primary Tubular Cells. DNA extraction from allograft biopsy and donor derived cell culture. NGS panel sequencing, analysis of polymorphic markers by STR.
Results: We report the multi-organ donation of a young patient with a rare ciliopathy, deceased by intracranial bleeding. Molecular diagnosis was performed by culturing donor tubular cells from the kidney recipient urine more than 10 years after transplantation, unraveling a novel truncating mutation of *OFD1*. Despite this severe donor disease, life-saving transplantation with good long-term outcome was enabled for five recipients. The route to diagnosis was more effective and reliable by the donor-derived cell culture as compared to an allograft biopsy.
Conclusion: The reported case of postmortal organ donation is a telling example of difficult decision making, in particular for acceptance of kidney allografts. The molecular diagnosis of the donor disease was performed by analyzing cultured cells from the kidney allograft derived from the urine, more than ten years after death of the donor. Despite the existence of a rare ciliopathy, organ donation led to life-saving transplantation of five recipients. This is true even for the two kidney recipients, though the donor disease itself can lead to end-stage renal disease. Thus, the reported case is a marked example of a medical borderline situation leading to successful organ utilization.

PV029 PREGNANCY AFTER RENAL TRANSPLANTATION

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Introduction: Pregnancy after renal transplantation (tx) means a risk for mother, child, and the renal graft.
Methods: We evaluated the course and complications of all pregnancies after renal transplantation since 1973 in Hannover by reviewing the records for complications regarding outcome of the child as well as renal function and graft survival of the mother.
Results: We found 62 women with 85 pregnancies and 88 deliveries. Four women (6.5%) lost their graft by pregnancy; 2 by haemolytic-uremic syndrome; 1 by severe preeclampsia; 1 by severe rejection (stopping immunosuppression). Complications during pregnancies were preeclampsia-related problems (29.6%), urinary obturation (8%), rejection (5%), intrahepatic cholestasis (6%), and strangling by the umbilical cord (3%). 68.2% of children were born by cesarean section. Seven children (8%) died before or shortly after birth (late interruption of a twin pregnancy because of medical reasons; severe retroperitoneal bleeding of the mother; placenta problem; preeclampsia; unknown reason). The age of the mothers at tx was 23.9 ± 8.9 and at delivery 30.8 ± 8.8 years; the time period from tx up to childbearing was 7.2 ± 5.7 years after tx (0.8 – 28.3 years). Renal function (eGFR CKD-epi-creat) before pregnancy was 59 ± 23 mL/min; % loss of eGFR by pregnancy was 15 ± 21% (0–86%). The children were born at gestation week 34 ± 12; the birth weight of the children was 2502 ± 3157 g. The % loss of eGFR by pregnancy correlated with the time up to graft failure after delivery (n = 28, R = −0.55, p = 0.005); eGFR before pregnancy correlated with % loss of eGFR after pregnancy (n = 76, R = −0.268, p = 0.02), with the gestation week at delivery (n = 76, R = 0.457, $p < 0.0001$), and with the time up to graft failure after delivery (n = 29, R = 0.371, p = 0.04). Ten mothers (16.1%) died during the observation time 1–21 years after pregnancy (infection 3, heart failure 2, coronary heart disease 1, malignancy 2, intraperitoneal bleeding 1, accident 1).
Conclusion: Women after renal tx have a risk to lose their graft during pregnancy and to die of various reasons before their children are adult. Renal

function before pregnancy plays a key role for a good outcome of the mother and her graft as well as for the child.

PV030 KIDNEY GRAFT SURVIVAL OF >25 YEARS: A SINGLE CENTER REPORT INCLUDING ASSOCIATED GRAFT BIOPSY RESULTS

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Introduction: Only few centers have reported their observations on patients with very long-term kidney graft survival of more than 25 years.
Methods: Eighty-six patients were identified in our center with graft survival of > 25 years and for 72, sufficient data were available, which we report in this study.
Results: Age at transplantation was 29.4 ± 12 years. Donor age was 31.3 ± 18.5 years. Mean duration of transplantation was 30.3 ± 3.6 years. At last follow-up, the cystatin C clearance was 47 ± 23 ml/min. Median urinary protein excretion at the last follow-up visit was 70 mg/l. The cystatin C clearance correlated inversely with proteinuria ($r = -0.46$, $p = 0.002$). Transplant biopsies for cause were performed in 30 patients at a median of 28.4 years (19.1–40.3) after transplantation. Acute or chronic active T cell-mediated rejection was present in 5 cases and histological characteristics of acute or chronic active humoral rejection in 8 cases. In patients with humoral rejection, donor-specific antibodies were detected in 2 cases and non-donor anti-HLA antibodies in the remaining 6 cases. More than 80% of biopsies had inflammatory infiltrates in non-atrophic or atrophic cortical areas but only 2 cases fulfilled all criteria for chronic T cell-mediated rejection. The number of HLA mismatches was higher in biopsied patients (3.0 ± 1.8 vs. 2.2 ± 1.7 without biopsy). Besides in patients with rejection, in further 14 patients the total-i score was positive. Arteriolar hyalinosis of differing degrees were present in all patients, but severity was not specifically linked with blood pressure, diabetes or calcineurin inhibitor therapy. Immunosuppressive therapy was adapted in most biopsied patients

impaired graft function and proteinuria was unchanged at last follow-up. 60% of all patients had hyperparathyroidism (iPTH of the whole group: 132 ± 157 pg/ml), which was predominantly secondary, as judged by serum calcium and graft function.
Conclusion: Young donor age was certainly a prerequisite of long-term graft survival. Nonetheless, inflammation or rejection in most biopsied patients suggests an important role of alloreactivity even in this late course.

SHORT POSTER PRESENTATIONS IV: HEART/LUNG

PV031 THE FREQUENCY OF TISSUE-RESIDENT DONOR T AND NK CELLS IN PERIPHERAL BLOOD AFTER LUNG TRANSPLANTATION IS MODULATED BY NORMOTHERMIC EX VIVO LUNG PERFUSION

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Introduction: The appearance of passenger donor lymphocytes in recipient blood after lung transplantation has been described decades ago. However, neither their early kinetics, nor distribution of lymphocyte subsets and clinical relevance has been addressed in detail. Therefore, we investigated frequencies and phenotypes of donor T and NK cells within the first 24 hours and at 3 weeks after lung transplantation and correlated those to clinical outcomes.
Methods: Blood and perfusion solutions of 59 lung recipients (30 male, 29 female, median age 51) were analysed pre Tx, at T0, T24 and at 3 wk. In a subset of 20 patients with standard cold donor lung preservation and 9 preserved with portable ex vivo lung preservation (OCS Lung), donor T/NK cells were identified in blood by staining of donor HLA epitopes (HLA-A1,A2, A11,A24) combined with lineage markers. Frequencies of donor lymphocytes were correlated to cold ischemic time (CIT), primary graft dysfunction (PGD) and chronic lung allograft dysfunction (CLAD).
Results: In all lung recipients, NK cell frequency was significantly increased at T0 and T24 ($p = 0.04$), CD4 T cells decreased and CD8 T cells remained stable. No significant differences were seen between recipients of standard vs OCS preserved lungs. Donor NK cells comprised 18.8% at T0, 17.1% at T24 and 7.8% at 3 wk ($p < 0.001$) of circulating NK cells. Frequencies were for donor CD8 + T cells 8.3%, 6.6% and 2.6%, and for CD4 + donor T cells 6.4%, 4.6% and 1.3% of the respective subset. At T0, significantly less donor NK cells were detected in recipients of OCS lungs ($p < 0.008$), while T cells were reduced non-significantly. No correlation between donor NK/T cell frequencies was observed for CIT or PGD. In the limited number of patients at risk, a trend towards higher early donor T cell frequencies in recipients not developing CLAD at 2 yrs after Tx was observed.
Conclusion: Donor T/NK cells are detectable in blood of all lung recipients during the first 3 wk after Tx and did not correlate with CIT or PGD. Preservation with portable EVLP resulted in decreased NK cell frequencies which might be explained by their ex vivo mobilization. Transient donor chimerism might have a protective effect against CLAD development.

PV032 EX VIVO LUNG PERFUSION USING THE PORTABLE OCS MAINTAINS ENDOTHELIAL INTEGRITY IN THE CONTEXT OF REDUCED SEVERE PGD RATES

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Introduction: The INSPIRE trial revealed significant reduction of PGD grade 3, i.e. less ischemia reperfusion injury (IRI) using the Organ Care System (OCS) compared to controls for lung preservation. In order to investigate endothelial mechanisms initiated by cold vs. normothermic preservation, blood and perfusates of INSPIRE patients were assessed for proteins involved in endothelial integrity. We hypothesized that OCS preservation also supports endothelial integrity in parallel to an anti-inflammatory milieu.
Methods: Blood plasma pre, T0, T24 post Tx and perfusion solutions from 33 OCS and 26 SOC patients with control-preserved lungs were analysed for 100 cytokines, angiogenic factors, etc. by multiplex assays. Donor and recipient demographics, cold ischemic times and PGD scores were assessed and correlated with protein levels.
Results: Clinical evaluation (OCS/control) revealed mean total cold ischemic times (CIT) 258 ± 6 vs. 549 ± 22 min ($p < 0.0001$). In the OCS group, no cumulative PGD score > 2 was observed compared to 19% PGD3 in SOC ($p = 0.035$). Less IRI in OCS patients was shown by significantly reduced IL-6, CXCL8, CXCL10, CCL2 plasma levels at T0. OCS plasma levels at T0 were also significantly lower for sCD31 ($p = 0.002$), ICAM-1 ($p = 0.025$), PAI-1 ($p = 0.03$), leading to a higher PAI-1/uPA ratio of 82 in OCS compared to 67 in SOC. Lower VCAM-1, IGFBP-1, Ang-2, uPA, sHer2/neu, sVEGFR2 levels were detected in OCS compared to SOC recipients but did not reach statistical significance. Plasma levels of endoglin (CD105, $p = 0.01$), PlGF ($p = 0.02$) correlated with CIT. In contrast to the PGD correlation to IL-6 in SOC patients, none of these proteins showed a PGD correlation at T0 or T24. In contrast to plasma, significantly higher concentrations of these proteins were measured in OCS vs. SOC perfusates ($p < 0.01$).
Conclusion: During normothermic lung preservation using the OCS system, reduced IRI is accompanied with protection of the endothelium, which can be detected by lower T0 plasma levels of endothelial activation markers. Thus, lung preservation using the OCS initiates an anti-inflammatory cascade and a tissue-protective milieu resulting in improved graft function.

PV033 DONOR LYMPHOCYTES IN THE PERIPHERAL BLOOD OF PATIENTS AFTER LUNG TRANSPLANTATION ARE COMPRISED BY HIGH FREQUENCIES OF KILLER CELL IMMUNOGLOBULIN-LIKE RECEPTOR-POSITIVE T AND NK CELL SUBSETS

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Introduction: For end-stage lung diseases, transplantation (Tx) is the only curative treatment option. However, acute and chronic rejection are major problems in Tx medicine. Thus, a better understanding of the contribution of immune responses early after Tx is urgently needed. The main proportions of passenger cells, derived from donor lungs and migrating into the recipients' periphery, are donor T/NK cells. As a part of the innate immune system donor NK cells in lung tissue predominantly show a $CD16^+$ $CD56^{dim}$ phenotype and express a specialized repertoire of inhibitory receptors, so called Killer Cell Immunoglobulin-like Receptors (KIR). Therefore, our aim was to characterize this KIR repertoire regarding differences between donor and recipient NK/T cells in recipient blood after DLTx. Furthermore, we want to analyze the functional capacity of these donor cells.
Methods: Blood samples at T0, T24 and 3 wk post Tx of 14 DLTx patients were investigated for the presence of donor cells using specific staining of HLA mismatched alleles and for differences between donor and recipient cells regarding their KIR repertoire and activation markers (CD25) via flow cytometry.
Results: Within the first 3 wk after DLTx, donor T/NK cells were detected in all patients with a peak at T0. An increase of a KIR2DL1 and KIR2DL2/3 positive

subset was detectable on donor NK cells (KIR2DL1 $p < 0.05$). Moreover, donor NK cells show significantly higher frequencies of KIR2DL2/3 ($p < 0.01$) on their surface 3 wk post Tx compared to the recipient. This effect can also be seen on donor T cells within the first 3 wk after LTx (KIR2DL1 $p < 0.05$; KIR3DL1 $p < 0.01$). CD25 expression as functional marker showed an earlier activation of recipient NK cells compared to donor NK cells.
Conclusion: The higher frequency of donor T/NK cells expressing inhibitory receptors like KIR on the surface compared to recipient cells indicates that they were derived from lung as a specialized compartment. Based on this KIR expression, the threshold for activation may be higher resulting in a poor response towards the allogeneic setting. Hence, T/NK cells might have a positive effect on tolerance induction and graft survival after LTx.

PV034 CLASSIFICATION AND CARE OF DRIVELINE EXIT WOUNDS AFTER VAD IMPLANTATION

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Introduction: Ventricular assist devices (VAD) are a routine treatment for patients with end stage heart failure. Results are impaired by driveline and pocket infections. The aim of this study was to analyze our institutional rate of infections and present a classification and treatment plan.
Methods: In a single center, retrospective analysis 197 patients after consecutive left ventricular assist device (LVAD) implantation (2010 to 2018) were identified and 123, treated exclusively at our hospital, were included in the study.

We developed a standardized classification, documentation and treatment plan as well as a standardized team training led by specialized technicians (ST). Patients, relatives and general practitioner were supported with all relevant hygienic aspects. All hospitalized and ambulatory patients were included in a database with wound status, therapy, photo and microbiological documentation. Frequency of controls was adjusted to wound status. Grade1 and 2 wound care was performed by nurses. For grade 3 and more ST were responsible.
Results: Out of 123 patients 1814 wound controls were performed

Driveline wound classification (Percentage value) - Therapy

GRAD 1: no irritation (49.5%) - dry dressing with silver wound dressing (Metalline)

GRAD 2: redness (23.4%) - Hydrogel with silver wound dressing (Metalline)

GRAD 3: secreting (6%) - dry dressing with suction pad (Trionic)

GRAD 4: redness, secreting (9.5%) - dry dressing with alginate-dressing

GRAD 5: redness, purulent, Secretion (8.7%) - wound lavage with daily dressing changes

GRAD 6: redness, wound healing deficit (1.7%) - individually

GRAD 7: redness, secretion, wound healing deficit (2.6%) - individually, surgical

Conclusion: A standardized concept for the care of driveline exit wounds is necessary in the hospital and especially for ambulatory patients. Under these circumstances the number of surgical interventions is extremely low, high urgent transplantation can be avoided and most driveline exit wound heal without problems.

PV036 LINKING EARLY HUMORAL SENSITIZATION IN LUNG TRANSPLANT RECIPIENTS WITH EARLIER CELLULAR ALLOREACTIVITY IN HUMANIZED MICE

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Introduction: The ability of donor-specific major histocompatibility complex alloantibodies (DSA) to destroy a transplanted organ through their cytotoxic effect has been known for a long time. Here, we studied the influence of DSA on clinical lung transplant recipients (LTR) in a humanized mouse model of transplant arteriosclerosis (TA) and attempted to control these by boosting putative Treg counts.
Methods: The pericardiophrenic artery was procured from surplus tissue of donor lungs transplanted in our clinical program and was implanted into the abdominal aorta of immune deficient mice. Nine patient (47%) developed DSA early after lung. Ten patients (52.6%) were tested having no DSA after lung transplantation (LTX). Mice were divided into four treatment groups. Group A mice received no human leukocyte reconstitution and served as negative controls. Group B mice received 5×10^6 allogeneic human peripheral blood mononuclear cells (PBMC DSA+) from the respective DSA positive LTR. Group C mice received PBMC from the respective DSA positive patients enriched with additional $CD4^+$ $CD25^{high}$ cells representing putative Treg. Group D mice received PBMC from DSA negative patients(PBMC DSA-). Group E mice received PBMC DSA-. enriched with additional $CD4^+$ $CD25^{high}$ cells.
Results: The control group A showed only mild thickening of the intima ($11.66 \pm 11.62\%$). In group C, reconstituted with alloantigen-primed PBMC, intimal thickening resulting in obliteration of the vessel lumen was significantly more severe than in group B, reconstituted with naïve PBMC (33.08 ± 24.58 vs. $50.29 \pm 21.03\%$, $p = 0.005$). By contrast, in group D, reconstituted with naïve allogeneic PBMC enriched with $CD4^+$ $CD25^{high}$ cells, intimal thickening was significant less severe than in group B (3.88 ± 18.88 vs. $33.08 \pm 24.58\%$, $p = 0.012$). In group E, enriching alloantigen-primed Treg similarly suppressed TA elicited by alloantigen-primed PBMC (0.16 ± 22.52 vs. $50.29 \pm 21.03\%$, $p = 0.0009$).
Conclusion: We conclude that alloantigen priming in clinical LTX recipients leads to more severe TA in a humanized mouse model. Intriguingly however, TA elicited by naïve allogeneic PBMC and by alloantigen-primed PBMC is similarly controlled by putative Treg.

PV038 IMMUNOLOGICAL EFFECTS OF INTRAVENOUS IMMUNOGLOBULINS ON T-CELLS

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Introduction: Immunoglobulins (IVIG) are nowadays widely used to treat humoral rejection in patients after solid organ transplantation. However, the exact mechanisms of IVIG treatment are unclear. It was the aim of this study to characterize the immunological effects of IVIG treatment.
Methods: Nine patients with humoral rejection after lung transplantation were enrolled. All patients received IgM-enriched IVIG over up to four consecutive days at a cumulative dosage of 60–80 g. Eight patients underwent plasmapheresis prior to IVIG administration. Blood was drawn before IVIG administration. Six patients were sampled again after IVIG administration. The mean time between first and last blood sampling was three months. PBMC were isolated from whole blood and T-cells were analyzed by flow cytometry.
Results: Regulatory T-cells ($CD4^+$ $CD127^{low}$ $CD25^+$) increased slightly after IVIG treatment ($5.23 \pm 1.8\%$ vs. $6.52 \pm 3.9\%$, $p = 0.3$); the same tendency was observed for activated T-cells ($CD3^+$ HLA-DR^+). In contrast, CD8 effector T-cells ($CD8^+$ $IFNg^+$, $50.66 \pm 20.00\%$ vs. $39.02 \pm 16.83\%$, $p = 0.3$) tended to decrease after IVIG treatment. Interestingly, CD8 effector T-cells producing IL-10 ($CD8^+$ $IFNg^+$ IL-10^+) were found in 66% of the patients after IVIG treatment. IL-10 producing CD8 T-cells were not found in patients before IVIG administration.
Conclusion: IgM enriched IVIG treatment may induce the development of IL-10 producing cytotoxic T-cells.

PV039 HISTOMORPHOLOGY AND MOLECULAR MECHANISMS IN ACUTE AND CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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Introduction: Alloimmune reactions represent – besides various infections – the major cause for impaired lung allograft function following transplantation. Acute cellular rejection (ACR) is not only a major trigger of acute allograft failure, but also contributes to development of chronic lung allograft dysfunction (CLAD).
Methods: We reviewed the most recent consensus on lung transplant pathology and newest molecular findings and combined these findings with our institutional expertise for a comprehensive overview of lung transplant pathology.
Results: So far no clinical testing alone allows for the determination of the possible causes of lung function impairment of lung transplant (LuTx) patients,

thus histopathologic assessment of post-transplant lung biopsies is a main element of the interdisciplinary diagnostic work up and correct treatment of both, acute graft rejection and chronical failure. Furthermore, differential diagnosis of ACR against infections or post-transplant lymphoproliferative disorder can be challenging by conventional histopathology. Therefore, specialized histological tools such as immunohistochemistry and molecular pathology can significantly improve the diagnostic reliability regarding differentiation between alloimmune reactions and infections or other causes.

Analogous to other solid organ transplantations, acute antibody mediated rejection (AMR) has become a recognized entity in lung transplantation pathology requiring comprehensive analysis of clinical, serological, microbial and histopathologic results for its correct diagnosis.

In view of these increasing challenges, fundamental research on the underlying molecular mechanisms recently progressed resulting in several approaches for predictive diagnostic tools for the early diagnosis of acute and chronic lung allograft dysfunction. However, until now, no thoroughly reliable predictive and prospectively evaluated tool has been established.

Conclusion: Here, we provide a comprehensive overview of lung transplant pathology with special emphasis on the histopathology of graft dysfunction and new findings regarding molecular pathways of acute and chronic graft dysfunction.

PV040 LUNG TRANSPLANTATION IN PATIENTS WITH SEVERE PULMONARY HYPERTENSION –FOCUS ON RIGHT VENTRICULAR REMODELING

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Introduction: This study was meant to analyse the centre experience of the Munich Lung Transplant Group in lung transplantation of patients with severe pulmonary hypertension. Outcome data focus on survival and right heart remodeling.

Methods: All patients receiving a lung transplant between 10/2010 and 08/2016 were retrospectively analysed ($n = 343$). Patients were categorised into individuals with or without severe preoperative pulmonary hypertension (PH; mPAP $\geq$ 35 mmHg or mPAP $\geq$ 25 mmHg with cardiac index $<$2.0 $L \cdot min^{-1} \cdot m^{-2}$). Among those, patients with severe PH secondary to lung disease (Nice Class III) were compared to patients with severe PH due to idiopathic PH (IPAH; Nice Class I). All surviving patients with severe PH were electively followed up by echocardiography.

Results: Kaplan-Meier survival probabilities after lung transplantation of each group according to preoperative mPAP values showed no statistically significant difference ($p = 0.14$ by log-rank test). Lung transplantation in severe PH patients yielded in marked right ventricular remodeling as indicated by significantly increased Tricuspid Annular Plane Systolic Excursion (TAPSE) ($p = 0.002$), decreased right ventricular end-diastolic dimensions ($p = 0.001$) and overall reduction of tricuspid valvular regurgitation, when compared to preoperative assessments.

Conclusion: Sequential bilateral lung transplantation (BLTx) in patients with severe pulmonary hypertension is a feasible treatment option in this high-risk group in experienced high-volume centres. Lung transplantation allows for resolution of secondary right heart failure in these patients.

SHORT POSTER PRESENTATIONS V: IMMUNOLOGY/ IMMUNOSUPPRESSION

PV041 GRAFT VERSUS HOST DISEASE AFTER LIVER TRANSPLANTATION- A REMINDER OF ITS EXISTENCE

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Introduction: Graft versus host disease (GVHD) is a well-known complication after bone marrow or stem cell transplantation. After solid organ transplantation however, it is very rare. The incidence increases with the number of hematopoietic cells that are transplanted with the organ, it is more common after small bowel transplantation. We know that some hematopoietic cells such as monocytes and macrophages are transplanted with the liver. These however are considered as tolerogenic on the hosts immune system preventing rejection. There are a few cases of GVHD reported in the literature with a very poor outcome. We here present one case after liver transplantation early this year.

Methods: Our Patient was transplanted at the age of 46, with the underlying diagnosis of PBC. He qualified for standard exception listing raising his laboratory MELD score from 25 to 28.The donor was a 19 year old female, died of cerebral anoxia with a DRI of 1.2. The initial course after transplant was uneventful, the patient was discharged from ICU at day 4. Approximately 12 days after transplant he developed fever, joint pain and diarrhea. We screened for bacterial, fungal and viral infections, by CT Abdomen, blood culture, stool culture, colonoscopy with biopsies, urine culture, septifast and serology without any positive findings. Nevertheless we suspected a viral infection and commenced antiviral treatment. Only after the patient did not improve, GVHD came into our mind as differential diagnosis.

Results: Diagnosis was confirmed by our pathologists in mucosal biopsies by lymphocyte invasion and apoptosis. Skin biopsies showed second degree GVHD. After retrieving native donor and recipient DNA we could even diagnose a macrochimerism of $>$ 10% in the peripheral blood. The patient was then started on high dose steroid treatment and improved markedly. He is currently still on our ICU so we cannot report of any outcome.

Conclusion: Since graft versus host disease is very rare after liver transplantation, it is seldom considered to be a differential diagnosis for the above mentioned symptoms. If diagnosed early enough some fatal cases could be prevented by initiating the correct treatment on time, maybe improving outcome.

PV042 IMPACT OF HLA-G GENE POLYMORPHISMS ON ACUTE REJECTION AFTER KIDNEY TRANSPLANTATION

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Introduction: Human leucocyte antigen G (HLA-G) is a non-classical HLA-class Ib antigen. It has been described that HLA-G plays a role in promoting and maintaining tolerance in pregnancy and after organ transplantation by downregulation of the innate and adaptive immune response. The polymorphisms 14-base pair (bp) insertion/deletion (ins/del) (rs1704) and +3142C>G (rs1063320) are of crucial importance for HLA-G expression.

Methods: We genotyped 175 kidney recipients (41 with acute rejection, and 134 without rejection) and additionally the corresponding donors for both polymorphisms in order to assess their impact on acute rejections one year after kidney transplantation. In addition, we analyzed soluble HLA-G (sHLA-G) levels in sera of 32 living kidney donors and compared the sHLA-G serum levels in terms of the analyzed HLA-G polymorphisms.

Results: In kidney transplant recipients we did not observe any association between 14-bp ins/del and the + 3142C>G polymorphisms and acute kidney transplant rejection. In contrast, we found a higher frequency of the genotypes 14-bp ins/ins and + 3142GG in donors of the no-rejection kidney allograft recipient group compared to the rejection group (4.9% vs. 24.6%; $p = 0.004$; 9.8% vs. 31.3%; $p = 0.008$) indicating an association. Soluble HLA-G levels were highest in healthy kidney donors homozygous for the 14-bp insertion.

Conclusion: We conclude that the HLA-G polymorphisms of the donor are of importance for susceptibility of acute rejection in kidney transplantation. We suggest that the donor 14-bp ins/ins and the + 3142GG genotypes acting protective against kidney transplant rejection.

PV045 PERSONALIZED IMMUNOSUPPRESSION AFTER TRANSPLANTATION REALIZED BY T-CELL MONITORING VIA ELISPOT

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Introduction: Individual Immunotherapy for patients after transplantation has been moved more and more into the focus of physicians and transplant centers, as individualized therapy approaches enable to minimize long-term side effects and increase the quality of life for the patients.

These individual therapy approaches require high demands on diagnostics and therapy monitoring as well the detection of new Biomarkers.

Methods: The Enzyme-Linked ImmunoSpot assay (EliSpot) has become a powerful tool in solid organ and stem cell transplantation. In a Europe-wide multicenter study, the Bio-DrIM project (BIOmarker-Driven personalized

Immunosuppression©), the use of the EliSpot method has been extensively evaluated to elect kidney transplant recipients for personalized therapy.

The reference institute established SOPs and trained the attending sites to meet the stringent requirements. EliSpot Reader Systems and EliSpot kits were extensively technical validated to guarantee that all centers reach the same results.

Results: A total of 21 plates from 4 different lots, processed by 5 operators, with 1983 wells were counted. Linear regression of all 1983 pairs of values lead to a linear regression line with the equation $y = 1.026 * x + 0.06888$ and a Pearson correlation coefficient $R^2 = 9988$, demonstrating the high concordance of each reader system.

To further demonstrate the extraordinary high standardization of the procedure, Inter- and Intra- Assay evaluation were performed by 5 different operators, 3 different lots on 3 different days, respectively, 2 operators performed 11 assays including 3 replicate wells for each antigen using cells isolated from 3 buffy-coats and one fresh blood sample. Depending of the number of spots in the set of analyzed results the CV % varied under 20%, which is far below cellular assays specified by the FDA with 25%.

Conclusion: In conclusion, the powerful combination of the EliSpot method with the EliSpot Reader System is a high-performance tool for diagnostics and monitoring of immunosuppression. Based on the high standardization potential, this state-of the-art technology will play an important role in diagnostic validation of next generation personalized therapy.

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PV046 GRAFT-VERSUS-HOST DISEASE FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION. IS THERE A NEED OF PARADIGM SHIFT IN IMMUNOSUPPRESSIVE THERAPY?

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Introduction: Graft-versus-host disease (GvHD) following liver transplantation (LTX) is a rare but fearsome complication. Currently, there are limited data regarding risk factors, diagnosis and management of GvHD following LTX and no recommendation exists regarding its management. We hypothesize that reduction of immunosuppression might improve outcome by strengthening the host's immune system in order to reduce the present high mortality rates in patients suffering of GvHD following LTX.

Methods: Systematic review of studies reporting GvHD following LTX was performed using PubMed and Medline databases. The medical subject headings *graft-versus-host disease, GvHD,* was used in combination with *liver transplantation.* 109 articles reporting 197 patients and their survival after diagnosis and therapy of GVHD following orthotopic liver transplantation were identified.

Results: 23 patients without information about prior immunosuppression or alternation of immunosuppression after diagnosis of GvHD as well as 6 patients with occurrence of GvHD after liver retransplantation were excluded.168 patients suffering from GvHD following LTX were included.

Overall survival was 27% ($n = 45$). 22 patients (13%) were treated with a reduction of immunosuppression after diagnosis of GVHD. In these, overall survival was 48%, compared to 22% in patients with an escalation of immunosuppressive therapy. Subjects treated with methylprednisolone pulses ($n = 25.15\%$) showed a survival rate of 40%.

Conclusion: This systematic review indicates for the first time that GvHD following LTX is best treated by reducing immunosuppressive burden most likely by allowing host- immunocompetent cells to counteract GvHD.

PV047 PROMOTING ADHERENCE: A ONE YEAR SINGLE-CENTER FOLLOW-UP USING A TACROLIMUS PROLONGED RELEASE AGENT (*ENVARSUS*®) FOR LONG-TERM IMMUNOSUPPRESSION IN PATIENTS AFTER LIVER TRANSPLANTATION

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Introduction: Calcineurin inhibitors are an essential pillar within immunosuppressive regimes following organ transplantation with tacrolimus being the most common drug in this field. *Envarsus*®, a prolonged tacrolimus release agent, was designed to permit an overall dosage reduction due to an enhanced bioavailability. As a once-daily drug, it might moreover increase patient compliance and adherence. We here present interim results from a single-center *Envarsus* trial in liver transplant patients.

Methods: 165 patients (males: 51%, females: 49%) with a history of liver transplantation (mean: 5.0 years, [0.4–28.5]) were switched from *Prograf* (median dosage: 2 mg/day, [0.75–15]) to *Envarsus* applying a 1:0.7 ratio. Follow-up examinations were conducted 1, 3, 6 and 12 months after conversion and entailed blood tests, physical examinations and the BAASIS questionnaire including a visual analog scale (VAS) for self-reported adherence.

Results: While 22 patients dropped out for various reasons, 86.7% remained on *Envarsus* throughout the observation period after conversion. According to the VAS, a significant increase of patient compliance could be observed after both, 6 and 12 months ($p = 0.001$). Even though the daily tacrolimus dosage was reduced by 24% (2.3 mg to 1.75 mg), no episode of acute rejection occurred. Moreover, liver, kidney and metabolic parameters did not show any significant changes.

Conclusion: Tacrolimus prolonged release agents may increase patient adherence and reduce the overall oral dosage needed to treat. Further studies need to investigate long-term effects.

PV048 EFFECT OF FOOD ON THE PHARMACOKINETICS OF ONCE-DAILY PROLONGED-RELEASE TACROLIMUS

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Introduction: To evaluate the effect of a standardized continental breakfast on the pharmacokinetics of prolonged-release tacrolimus (PR-Tac, Envarsus®) as compared to immediate-release tacrolimus (IR-Tac, Prograf®).

Methods: We conducted a randomized 4-way cross-over pharmacokinetic trial (EudraCT 2017-000410-32) in which healthy volunteers (18 females, 18 males) received single 5 mg doses as PR-Tac and IR-Tac, with and without a standardized continental breakfast (707 kcal; 30% calories from fat). The wash-out period between doses was at least 14 d. Tacrolimus concentrations were measured by liquid chromatography coupled to tandem mass spectrometry. CYP3A5 rs776746 polymorphism and CYP3A4 phenotype (using a midazolam microdose) were assessed and tacrolimus pharmacokinetics was analysed using non-compartmental methods and mixed-model ANOVA.

Results: Breakfast decreased average tacrolimus exposure (AUC) with both preparations. The AUC was reduced to 67% (90% CI 59–75; $p < 0.01$) with IR-Tac versus 79% (70–89; $p < 0.01$) with PR-Tac, with a non-significant difference between both preparations ($p = 0.10$). Maximum concentration (C_{max}) and time to C_{max} (t_{max}) were significantly affected only after IR-Tac: C_{max} was decreased to 39% (34–45; $p < 0.01$) while t_{max} was 2.12-fold longer (1.79–2.52; $p < 0.01$). After PR-Tac, C_{max} and t_{max} were unchanged (C_{max} 87% (76–101; $p = 0.11$), t_{max} 1.01-fold (0.86–1.20; $p = 0.89$)); which was significantly different between both preparations for C_{max} and t_{max} (both $p < 0.01$). The effects were similar in males and females. An effect of CYP3A5 genotype or CYP3A4 phenotype could not be detected.

Conclusion: Average tacrolimus exposure was reduced to a similar extent with both preparations, whereas C_{max} and t_{max} were only affected after IR-Tac. The effect of a standardized continental breakfast on PR-Tac was considerably smaller than previously reported effects of a high-fat breakfast. Nevertheless, PR-Tac should not be administered with breakfast on some days and without on others. If tacrolimus is administered with food every day (off-label), day-to-day variability might be less with PR-Tac because C_{max} and t_{max} are unchanged.

PV049 IMMUNOSUPPRESSION WITH GENERIC TACROLIMUS IN LIVER AND KIDNEY TRANSPLANTATION – A SYSTEMATIC REVIEW ON BIOPSY PROVEN ACUTE REJECTION AND BIOEQUIVALENCE

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Introduction: While rejection prevention with innovator Tacrolimus (Tac) is one of the key factors for long lasting graft function, the use of generic Tac is still under debate. Thus this study was designed to generate evidence for the effect of generic Tac in adult liver (LT) and kidney transplantation (KT) with focus on both biopsy proven acute rejection (BPAR) and bioequivalence.

Methods: A systematic literature search for trials comparing generic vs. innovator Tac was conducted accordingly.

Results: A total of 17 controlled studies (5 LT, 11 KT, 1 LT/KT) including 1413 patients were identified. 92.9% (13/14; 5/5 LT, 8/9 KT) of studies have reported same or lower BPAR with generics; however, only 33.3% (3/9; 1/2 LT, 2/7 KT) of (sub)studies show bioequivalence of generics according to the area under the curve (AUC), 55.6% according to the concentration maximum (c_{max}) (5/9; 2/2 LT, 3/7 KT).

The comprehensive review of 79 publications (21 LT, 58 KT) with a total of 30962 patients (5657 LT, 25305 KT) suggests cost effective generic Tac being comparable with innovator Tac in both clinically relevant and pharmacokinetic outcome data.
Conclusion: Data shown here provide clear evidence on the cost effective safe clinical use of generic Tac after both LT and KT.

PV050 CONVERSION OF FAST AND SLOW TACROLIMUS METABOLIZERS TO EVEROLIMUS AFTER RENAL TRANSPLANTATION

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Introduction: Conversion from tacrolimus (Tac) to everolimus (EVL) after renal transplantation (RTx) can lead to a favorable graft function. As it was shown that fast Tac metabolizers (C/D ratio < 1.05 ng/ml/mg) have a lower estimated glomerular filtration rate (eGFR) compared to slow Tac metabolizers (C/D ratio ≥ 1.05 ng/ml/mg) [1], we hypothesized that especially fast Tac metabolizer profit from a conversion to EVL.
Methods: We analyzed data of 34 RTx recipients (17 fast vs. 17 slow Tac metabolizers) who were converted to EVL one to 24 months after RTx. The initial immunosuppression consisted of Tac, mycophenolate, prednisolone and an induction therapy with basiliximab. During an observation time of 36 months after conversion from Tac to EVL, renal function and adverse effects were compared between the groups.
Results: Fast Tac metabolizers were switched to EVL 6.3 ± 5.3 months and slow metabolizers 6.6 ± 6.1 months after RTx ($p = 0.838$). eGFR did not differ between the groups at day 10, 1 month after RTX and at the time of conversion (baseline). After conversion the eGFR in all patients increased significantly to a comparable extend (fast metabolizers eGFR 36 mo: + 11.0 ± 11.7 mL/min/1.73 m², slow metabolizers eGFR 36 mo + 9.4 ± 15.9 mL/min/1.73 m² vs. baseline, all $p < 0.05$). There were no significant differences in the adverse effects between the groups.
Conclusion: After conversion from Tac to EVL eGFR values of all patients increased significantly with a tendency towards a higher increase in fast Tac metabolizers.
References: 1. Thölking G, Fortmann C, Koch R, Gerth HU, Pabst D, Pavenstädt H, et al. The tacrolimus metabolism rate influences renal function after kidney transplantation. PloS one. 2014;9(10):e111128.

SHORT POSTER PRESENTATIONS VI: ORGAN DONATION

PV051 ORGAN VIGILANCE IN GERMANY–MALIGNANCY TRANSMISSION FROM ORGAN DONOR TO RECIPIENT

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Introduction: Vigilance monitoring after OT includes Serious Adverse Events (SAE) and Serious Adverse Reactions (SAR). *SAE* are findings in the donor after OT that pose a *risk of harm* to the already transplanted recipients of the donor, e.g. malignancies. *SAR* refer to *harm that has occurred* to one/more recipients of the same donor and is suspected of being associated with the donor organ.
Methods: Analysis of all SAE/SAR related to malignant tumors (TU) from 7/2015–12/2017.
Results: 17 donor neoplasms (SAE) were found (table). 14 were detected in donor organs during preparation in the recipient center, after pathological exam of not transplanted organs/donor autopsy. In 3 cases retrospective evaluation of donor history or imaging of the donor prior to death led to tumor diagnosis. 4 reported TU resulted in preventive or therapeutic organ removal or partial resection in the recipient. One pleuramesothelioma was transmitted to 2 recipients, both died.

11 SAR were reported 2 weeks -16 years after OT. 1 known donor glioblastoma was transmitted to one recipient. He died 28 months after OT.

Donor origin of SAR was confirmed/probable for 10 recipient TU, possible for 2, excluded for 2 TU.

10 malignancy SAE/SARs related to foreign donors have been reported to the DSO, none of them resulted in transmission (table).

Table: tumor entities:
German donors
n = 17 SAE: 5 RCC, 3 NET, 2 lung can., 2 plasmacytoma, breast ca., lymphoma, melanoma metastases, pleuramesothelioma, history of thyroid ca.
n = 12 SAR: 6 RCC, 2 multiple lung lesions, angiosarcoma, glioblastoma, lung ca., liver metastases
Foreign donors
n = 10 SAE/SAR: 4 RCC, 2 angiosarcoma, choriocarcinoma, lymphoma, thyroid ca., NET
Conclusion: An occult donor pleuramesothelioma was transmitted to 2 recipients, a known donor glioblastoma to a third recipient, all died. Comprehensive, detailed reporting of SAE/SAR and international data collection are crucial for transmission risk assessment. These data are essential to minimize tumor transmission in the future.

PV052 PASSIVE TRANSFER OF HEPATITIS C ANTIBODIES BY KIDNEY TRANSPLANTATION FROM A SINGLE DONOR TO TWO RECIPIENTS

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Introduction: The introduction of direct acting antivirals (DAA) to treat Hepatitis C virus (HCV) infection changed policies of using grafts from donors tested anti-HCV pos. and HCV-NAT neg. Such grafts can be used after informed consent in HCV-NAT neg. recipients regardless of anti-HCV status. We report the first unexpected seroconversion of two kidney transplant (KTX) recipients without detection of HCV observed in Germany.
Methods: Fallbericht.
Results: The 37 years old female donor had a history of iv-drug-abuse (>15 years), abuse of other drugs, diabetes Type II and asthma. Donor screening revealed anti-HCV pos., HCV-NAT neg., anti-HCV-confirmed pos. Intraoperative liver biopsy showed portal fibrosis >= Grade 1.

Both kidney recipients were anti-HCV neg. before KTX. 3 and 5 months after KTX anti-HCV was positive in both recipients and persisted positive until last follow-up (8 months). Interestingly HCV-NAT was negative 2, 3 and 8 months after KTX with normal liver function test.

The post-KTX course of one recipient (59 years, male) was complicated by acute kidney injury due to excessive fluid-loss via a colostomy (Crohn-disease > 30 years) and a D+/R- CMV mismatch (Viremia). The other recipient (49 years female) had an uncomplicated post-KTX-course.
Conclusion: According to European and US recommendations HCV-NAT screening of the recipients should be performed when organs were transplanted from donor with high risk to rule out window-period infection of the donor despite negative donor HCV-NAT. Within this context seroconversion of both kidney recipients was observed without HCV-viremia at any time. This is most likely explained by transfer of donor passenger lymphocytes producing antibodies against HCV and not by HCV infection. This reactivity may persist for months as it is known from other cases of donor passenger lymphocyte transfer (e.g. peanuts allergy or erythrocytes-antibodies). This underpins best practice, that screening for pathogens in recipients shall not be restricted to serology but should include NAT testing as serologic results may be false negative due to immunosuppression, or false positive due to donor derived passenger lymphocytes temporarily.

PV053 APPRECIATING UNKNOWN DONORS AND THEIR RELATIVES WITH ANONYMOUS THANK YOU LETTERS

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Introduction: Transplant medicine connects unknown people through emotions like grief, consolation and gratitude. Despite prescribed anonymity and data protection regulations, these emotions exist, and seek ways to be expressed.
Methods: Since the amendment of the German Transplantation Law effective April 1, 2019, care of donor relatives beyond the donation is, for the first time, prescribed by law and henceforth among the responsibilities of Deutsche Stiftung Organtransplantation (DSO). Donor relative care aims to validate the

decision to donate and provide means to answer open questions. Furthermore, the new law sanctions the forwarding of anonymized thank you letters from organ recipients to donor families. These letters are the only way in which involved parties can express their emotions to each other, if only anonymously.
Results: Despite their feelings of grief and loss, donor families feel emotionally connected to organ recipients. To them, receiving a thank you letter from organ recipients is a strong sign and important validation of their decision to donate organs. Standard letters with anonymized information on the outcome of transplantation surgeries by organ procurement agencies do not adequately meet this need of appreciation of donor families. The results of a survey among donor relatives (2004–2017) in the DSO Mitte region confirm this. Of 703 relatives participating in the survey, 294 (48.2 percent) indicated their wish to receive a thank you letter from organ recipients. 205 (29.1 percent) even expressed the wish to contact them directly. Such contact is currently prohibited by law.
Conclusion: Gratefulness of organ recipients can be expressed in many ways. An anonymous thank you letter is one of them. Although the decision to write such a letter has to be completely voluntary and optional, organ recipients in Germany should be routinely informed about this option and the profound impact it can have. Oftentimes, the desire to write a thank you letter grows with time, and is finally acted upon years after the transplantation. Despite such delays, donor families consider such a letter their most valued form of appreciation.

PV058 LIVING DONOR LIVER TRANSPLANTATION OF HEPATITIS C-INFECTED DONOR TO HEPATITIS C-INFECTED RECIPIENT COMBINED WITH DIRECT ANTIVIRAL AGENTS-THERAPY

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Introduction: Nothing is known about chronic HCV-infection, antiviral therapy and living donor liver transplantation (LDLT)into chronic HCV-infected pediatric recipients. To increase the donor pool, we report a novel concept of antiviral direct antiviral agents-therapy (DAA) in combination with LDLT in a HCV-infected donor and recipient.
Methods: After the diagnosis of a pseudopapillary pancreas tumor in 2005 the girl (11 years) underwent a subtotal left pancreas resection with splenectomy 2015. Extended and irresectable hepatic metastasis were trans-arterial chemoembolized, with inadequate success in 2016. After extended staging with no extrahepatic tumor manifestation, our institutional transplant board indicated a LDLT in 2017. At the time of initial evaluation, the mother (36 years) had a viral load of 6.6 x 10^6 IU/ml and liver biopsy revealed a chronic, discrete interface hepatitis and mild fibrosis. After successful DAA-therapy (Epclusa) the HCV viremia was cleared, liver enzymes were normal and the liver biopsy showed a marked reduction of the steatosis. Consequently, no contraindication for LDLT was present.
Results: We performed LDLT in piggyback technique of the segments II, III, IV (639 cm^3). At the time of transplantation, the recipient had an HCV viral load of 2.8 x 10^6 IU/ml, with mild liver enzymes elevation. Three months post-transplant, the recipient was stable with an HCV-load of 1.5 x 10^6 IU/ml. After DAA-therapy the HCV viremia was cleared in the SVR 12 week, and HCV remained undetectable thereafter. A control liver biopsy revealed a 60% steatosis and mild fibrosis. One-year post-transplant liver enzymes were normal and the 1-year protocol biopsy showed a marked reduction of the steatosis to 20%, and noteworthy no signs of chronic liver injury or fibrosis. We performed an abdominal-MRI scan, that revealed a tumor free recipient one-year post-transplant.
Conclusion: We showed that a chronic HCV-infection is not a contraindication for LDLT. Further, we demonstrated that liver transplantation is feasible in a congenitally HCV-infected pediatric recipient, and after successful DAA therapy HCV remained undetectable. We strongly believe that this novel concept should be considered to increase the donor pool.

PV059 RIGHT DONOR NEPHRECTOMY IS RIGHT – SINGLE CENTRE RESULTS OF 121 RIGHT DONOR NEPHRECTOMIES

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Introduction: It is still controversial if right kidneys are as suitable for living kidney donation as left ones due to suspected higher vascular complications due to a short renal vein.
Methods: We evaluated the results of 202 living donor grafts performed between 2009 and 2017 via mini incision donor nephrectomy or retroperitoneoscopic donor nephrectomy. Side decision based on organ function and vessel anatomy. If function and anatomy was identical, side decision was based on the surgeon's preference. 60% (n = 121) of donations were right sided nephrectomies.

Donor and recipient characteristics of left and right sided nephrectomies were comparable regarding donor and recipient age and BMI. 9 of 81 recipients (11%) of a left graft and 17 of 121 recipients of a right graft (14%) were children. 17/81 (21%) left and 23/121 (19%) right grafts had more than one artery. No venous reconstruction was performed in any case.
Results: There were four primary non functions in the left sided graft group (5%) in two recipients of ABOi grafts (one with additional non-HLA antibodies, not known before transplantation), in one sensitized recipient most likely due to DSA (immediate memory recall after transplantation) and in one 77 year old recipient of a 72 year old graft due to an intima flap. In the right side nephrectomy group two primary non functions (2%) occurred due to severe cardiac insufficiency in one recipient (the graft gained function after 6 month) and ureter obstruction in a 8 year old child (good function after one week).
Conclusion: In conclusion right and left sided nephrectomies are safe regarding vascular complications in adult and pediatric recipients using a mini open or a retroperitoneoscopic approach. In 202 donor nephrectomies only one graft loss was caused by an arterial complication, no venous thrombosis occurred.

PV060 HAND-ASSISTED RETROPERITONEOSCOPIC (HARS) VERSUS OPEN LIVING-DONOR NEPHRECTOMY: THE MÜNSTER TRANSFORMATION AND EXPERIENCE

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Introduction: Living donor nephrectomy should have minimal impact on donors since it is being performed on healthy individuals. Therefore, we adapted from September 2018 our standard of procedure from open retroperitoneal to hand-assisted retroperitoneoscopic nephrectomy.
Methods: From September 2018 to May 2019 we performed 20 HARS living-donor nephrectomies and compared those to a 1:2 match-pair collective of 40 donors undergoing open nephrectomy. For Comparison, a match-pair analysis in terms of donor age and side of nephrectomy was performed. Choice of kidney to be donated was made only on bases of poorer side differentiated clearance, regardless of vascular anatomy. Primary outcome measures were surgical time and length of hospital stay.
Results: There was no conversion to open nephrectomy in HARS group. Donors mean age was 54 years. 65% of all 60 nephrectomies were left-sided and 35% right-sided. Surgical time did not defer in terms of harvested side. Mean surgical time differed significantly between both groups (HARS: 130 min versus open: 220 min, $p < 0.0001$). Length of hospital stay was significantly shorter in HARS group compared to open nephrectomy (mean 4.9 days vs 9.5 days, $p < 0.0001$).
Conclusion: HARS nephrectomy in kidney living donation is superior to open technique in term of surgical time and length of hospital stay.

SHORT POSTER PRESENTATIONS VII: KIDNEY/PANCREAS

PV061 CARDIOVASCULAR OUTCOME OF DIABETIC PATIENTS WITH SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION COMPARED TO SOLITARY KIDNEY TRANSPLANTATION

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Introduction: Coronary heart disease due to arteriosclerosis is the leading cause of death in kidney transplant (KT) recipients. In present study, we examined how arteriosclerotic risk profile (ARF) and echocardiographic findings changed in patients after simultaneous pancreas and kidney transplantation (SPK) compared to solitary KT.
Methods: In a cohort of 127 transplant recipients with functioning grafts who had received either SPK ($n = 100$) or KT ($n = 27$) caused to diabetic nephropathy during 1998 to 2016, we studied patient characteristics (e.g. age, diabetes type, dialysis time, cardiovascular pre-existing conditions or events, data on organ donor) and analyzed changes in ARF (characterized through HbA1c, BMI, mean arterial pressure (MAP), hypercholesterolemia) 1, 3 and 5 years postoperatively. Moreover we compared echocardiographic findings pre-transplant and during follow-up.
Results: We noted that in our cohort recipients of solitary KT compared to SPK were transplanted mainly due to type 2 diabetes and were characterized by higher age (60.5 vs. 43 years.) and more prominent previous history of cardiovascular illnesses. Prior cardiovascular events occurred therefore significantly rarer in SPK patients ($p = 0.04$). During follow-up period, there was no difference notable between both groups. Considering changes in ARF, we found that hypercholesterolemia ($p = 0.017$) and MAP ($p = 0.00$) were significantly better in the SPK patients. Interestingly it has to be pointed out that significantly less SPK patients were treated with a lipid-lowering medication (36% vs. 55.6%; $p = 0.022$). Most patients in both groups received antihypertensives; one third of SPK patients and one quarter of KT patients were treated with more than 3 antihypertensive drugs. Left ventricular ejection fraction (LVEF) and the incidence of hypokinesis postoperatively were significantly better in patients with SPK (no pre-transplant difference).
Conclusion: In our study population the cardiovascular risk profile related to hypercholesterolemia, MAP, LVEF and hypokinesis appeared to be improving in recipients of SPK compared to solitary KT. A study with a larger case number is needed to make predictions regarding cardiovascular events and graft survival.

PV063 COMPLICATIONS AFTER PANCREAS TRANSPLANTATIONS WITH EXOCRINE DRAINAGE THROUGH A DUODENODUODENOSTOMY VS. DUODENOJEJUNOSTOMY

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Introduction: Pancreas transplantation has mostly being performed via duodenojejunostomy (DJ). Since 2007 duodenoduodenostomy (DD) has become the leading modality of choice at our center. However, the discussion remains wide open as to which methodology brings less complications.
Methods: Between 2002–2017 363 pancreas transplantations (PT) were performed. There were 236 PTs using duodenoduodenostomy (DD) and 127 PTs using jejunal anastomosis (DJ). We retrospectively compared postoperative complications in both groups, focusing on the rates of bleedings, thrombosis and the number leading to graft-pancreatectomy. Aspects such as graft rejection, postoperative pancreatitis, and other surgical complications as well as mortality and other morbidities were also considered in our study.
Results: In the DD-group there were noticed 108 (46%) cases of complications. Postoperative graft thrombosis was encountered in 24 (10%) cases, leading to 20 (8.5%) cases of pancreatectomy. There were also 28 (11.9%) postoperative bleedings noted leading to 12 (5.1%) cases of pancreatic graft loss. In the DJ-group there were 62 cases (49%) of postoperative complications namely 18 (14%) thrombosis, leading to 18 pancreatectomies (100%). 12 bleedings (9.4%) were noticed in this group, leading to 1 case of graft-pancreatectomy. The majority of DJ-group complications (72%) with regards of thrombosis-associated pancreatectomies were observed in the first postoperative week.
Conclusion: In conclusion, DD provides a smaller number of thrombotic complications compared to DJ. DD provides easy access for endoscopic surveillance and biopsy. It has to be considered, that there is no significant difference in the overall five-year survival rates in both groups (DD 91.5% vs. DJ 91.3%).

PV066 THE IMPACT OF IMMUNOSUPPRESSION ON POSTOPERATIVE RENAL GRAFT FUNCTION AFTER GRAFT-UNRELATED SURGERY: A RETROSPECTIVE CONTROLLED COHORT STUDY

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Introduction: Physicians are faced with a growing number of patients after renal transplantation undergoing graft-unrelated surgery. So far, little is known about the postoperative restitution of renal graft function and the risk factors for a poor outcome.
Methods: One hundred one kidney transplant recipients undergoing graft-unrelated surgery between 2005 and 2015 were reviewed retrospectively. A risk analysis was performed and differences in creatinine, GFR and immunosuppressive treatment were evaluated. Additional, a comparison with a case-matched non-transplanted control group were performed.
Results: Preoperative creatinine averaged 1.88 mg/dl (0.62–5.22 mg/dl) and increased to 2.49 mg/dl (0.69–8.30 mg/dl) postoperatively. Acute renal failure occurred in 18 patients and 14 patients had a permanent renal failure. Significant risk factors for the development of postoperative renal graft dysfunction were female gender, a preoperative creatinine above 2.0 mg/dl as well as a GFR below 40 ml/min and emergency surgery. Patients with tacrolimus and mycophenolate mofetil treatment showed a significant lower risk of renal graft dysfunction than patients with other immunosuppressants postoperatively. Contrary to that, the risk of patients with cyclosporine treatment was significantly increased. Transplanted patients showed a significantly increased rate of postoperative renal dysfunction.
Conclusion: The choice of immunosuppressant might have an impact on renal graft function and survival of renal transplant recipients after graft-unrelated surgery.

PV067 BIOPSY FINDINGS AFTER DETECTION OF DE NOVO DONOR SPECIFIC ANTIBODIES IN RENAL TRANSPLANT RECIPIENTS – A SINGLE CENTER EXPERIENCE

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Introduction: Development of de novo donor specific antibodies (DSA) is associated with an increased risk of antibody mediated rejection and a substantial reduction of allograft survival. We hypothesized that detection of DSA should prompt an immediate biopsy even in absence of proteinuria and loss of eGFR and changed our center's standard accordingly.
Methods: Single center retrospective analysis of 170 renal transplant recipients with positive de novo DSA. N = 91 (53.5%) were undergoing allograft biopsy after detection of de novo DSA between 2014 and 2018 irrespective of proteinuria and course of eGFR. All biopsies were analyzed at the same pathological institute. Diagnosis of antibody mediated rejection was established according to Banff 2013 criteria.
Results: At the time of biopsy $n = 37$ (40.6%) had a proteinuria/creatinine ratio (PCR) > 0.3 mg/mg and $n = 32$ (35.2%) had a loss of eGFR > 10 ml/min in the past 12 months (PCR available in 89.0%, delta GFR in 91.2%). At this time, mean age was 50.3 ± 11.3, mean eGFR 30.1 ± 12.9 and mean time after transplantation 4.9 ± 5.3 years. 78.0% of the biopsies provided the diagnosis of rejection. Among those, criteria of antibody mediated rejection were met in 77.5%. Among those subjects undergoing biopsy without proteinuria or loss of eGFR > 10 ml/a, 26 (76.5%) had biopsy proven rejection (30.8% cellular rejection, 50.0% antibody mediated rejection, 19.2% combined).
Conclusion: The majority of subjects with de novo DSA reveal histological signs of rejection, even in absence of proteinuria and deterioration of graft function. Thus, it appears reasonable to routinely perform allograft biopsy after detection of de novo DSA in order to detect subclinical rejections.

PV068 DUAL KIDNEY TRANSPLANTATION – A SINGLE CENTER EXPERIENCE

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Introduction: Scarcity of kidneys grafts suitable for transplantation is still a major obstacle. Reliable parameters to predict graft function are not available; however, parenchymal mass and donor laboratory values correlate with graft function. To expand the donor pool, kidneys that would have been discarded as single graft, may be used as double grafts.
Methods: 202 Patients underwent kidney transplantation (KT) since November, 2016. Cadaveric KT (KT-C) was performed in a total of 158 pts. including 10 cases of dual KT (KT-CD). Further 38 living related KT (KT-L) and 6 simultaneous pancreas-kidney transplantations (SPKT) were performed. Median recipient age was highest with 71 years (51.8–76.9) in KT-CD compared with 56 years in KT-C, 49.6 years in KT-L, and 49.6 years in SPKT, respectively. The decision, whether a single or dual cadaveric graft was implanted, was based upon histological grading according to Remuzzi, both organ size and function, and donor age.
Results: Outcomes and general data after KT (KT-C, -CD, -L, SPKT) were compared. There was no significant difference in gender and follow-up time. Graft function rate was 95%, 90%, 94.7% and 100% after KT-C, KT-CD, KT-L and SPKT, respectively, after a median follow-up time of 430 days (28–920). Median creatinine censored by death and graft loss was 1.48 mg/dl (0.27–5.96), 1.38 (0.88–2.6), 1.45 (0.34–4.23) and 1.08 (0.81–2.07) after KT-C, KT-CD, KT-L and SPKT, respectively.
Conclusion: KT-CD is a valuable option to increase the donor pool. Similar results, when compared with single organ transplantation, indicate appropriate decision making. Nevertheless, KT-CD should be performed only in otherwise discarded kidneys. The potential of additional organs is estimated by 5–10% of DBD donors.

PV069 STAYING CLOSE TO THE KIDNEYS: CYTOMEGALOVIRUS AND PERIRENAL ADIPOSE TISSUE

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Introduction: Human cytomegalovirus (HCMV) infection is one of the most important complications after renal transplantation, presenting with i.a. colitis or pneumonia. HMCV is associated with worse graft as well as patient survival and shedding by urine is frequent. However, its renal host cells are still unknown. Last year Shnayder et al. reported a Genotype-Tissue Expression Project (GTEX) analysis of HCMV across the body. Most viral reads were in pulmonal tissue, followed by equally skin, blood, ovary and adipose tissue. Perirenal adipose tissue is not included in GTEX data. Therefore, we analysed its HCMV permissibility, as well as changes in coding and long non-coding RNA (lncRNA) expression after infection.
Methods: Tissue was obtained with ethics board approval. Perirenal adipose-derived mesenchymal stromal/stem cells (prASC) were isolated according to Baer et al. and infected with HCMV patient isolate Hi91 (Cinatl et al.) at a multiplicity of infection of 1. In addition, prASC were infected in the presence of ganciclovir (GCV, 10 μg/ml). After 96 hours immunostaining was performed for HCMV late antigen (gB/gpUL55 MoAb). Total RNA was extracted from additional replicates, cDNA synthesized and expression levels of selected targets quantified by real-time PCR in triplicate measurements.
Results: prASC show high permissibility for HCMV, which induces a strong cytopathological effect (CPE). Cells similar to neurons survive 96 hours of infection, although staining positive for HCMV late antigen too. Treatment with GCV did inhibit HCMV replication. Among the analyzed lncRNA "Tumor suppressor long noncoding RNA maternally expressed gene 3" (MEG3) was upregulated in infected cells, while coding transcripts of neuron markers like "Neurofilament Heavy" (NEFH) were also strongly elevated.
Conclusion: HCMV infects prASC, showing a strong CPE. Cells with a neurone similar phenotype survive 96 hours of infection, but stain positive for late antigen too. Among the upregulated lncRNA is MEG3, which is known to repress proliferation and promote apoptosis. Therefore, HCMV might induce apoptosis by changing MEG3 expression levels. Further studies are needed to clarify its role in prASC after HCMV infection.

PV070 PRACTICAL UTILITY OF VARIOUS SCORES FOR THE EVALUATION OF DECEASED DONOR KIDNEYS

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Introduction: Marginal organs have been associated with inferior graft and patient outcomes and several scores have been proposed for the evaluation of deceased donor kidneys in order to facilitate the best possible allocation combination and to improve graft and patient survival. We retrospectively validated their performance in predicting outcomes in donor kidney evaluation biopsies.
Methods: We retrospectively evaluated the records of 223 consecutive adult cadaver renal transplant recipients with donor evaluation biopsies. Taking into account donor and recipient clinical data and graft histopathology, we performed a retrospective explorative univariate analysis of graft function at 3 and 12 months and 1- and 3-years graft and patient survival for the following scores: Navarro (2011), Ortiz (2004), Balaz (2013), Lopes (2004), Snoeijs (2008), Remuzzi (1999), Nyberg (2003), Rao (2009), Foucher (2009), Schold (2005), Port (2002), Anglicheau (2008), 3-year-Leuven (2013), Irish (2010), KDRI/KDPI and EPTS.
Results: In our cohort of 223 patients, for 3- and 12-month graft function most of the scores performed well; performance for 1- and 3-year graft survival was best for combined clinico-pathological scores like 3-year-Leuven ($p = 0.032$ and $p = 0.008$, respectively). For one-year patient survival, combined clinico-pathological scores like 3-year-Leuven ($p < 0.001$) and Anglicheau ($p = 0.016$) performed as well as the purely clinical scores like KDRI ($p = 0.001$), Rao ($p < 0.001$) or Nyberg ($p = 0.001$).
Conclusion: Composite scores which also consider graft histology like 3-year-Leuven, Rao and Nyberg seem to be better suited to predict graft survival than purely clinical scores. For the prediction of patient survival, graft histology does not matter as much. These scores should be tested for their performance in a prospective multicentric study design.

SHORT POSTER PRESENTATIONS VIII: PSYCHOSOMATICS/ETHICS

PV071 PSYCHOLOGICAL AND BIOLOGICAL MARKERS FOR THERAPY ADHERENCE AND RELAPSE RISK IN PATIENTS WITH ALCOHOLIC LIVER DISEASE BEFORE AND AFTER LIVER TRANSPLANTATION: A PROSPECTIVE MULTICENTRE STUDY

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Introduction: Therapy adherence, craving and relapse are factors contributing to therapy outcome in patients listed and transplanted due to alcoholic liver disease (ALD). To improve therapy, it is essential to find psychological and biological parameters to assess those factors. Markers such as leptin show promising evidence for the assessment of craving. For the psychological evaluation of adherence and comorbidity reliable and valid questionnaires exist that are used in the context of transplantation medicine (1, 2). Nonetheless, no study has yet used a combination of such assessments in a longitudinal setting.
Methods: For our analysis, we want to include the following groups

- patients with ELC or end-stage ALD on the LTX waiting list (LTX group) ($n = 120$)
- patients with viral cirrhosis or NASH on the LTX waiting list (C-TX group) ($n = 120$)
- patients with alcohol use disorder who are abstinent (min. 6 months) and have normal liver values (C-AD group) ($n = 60$)

The period of patient acquisition will be two years. Initial psychiatric assessment of all patients will be followed by a somatic and psychological assessment every three months until LTX. After LTX, the patients will be seen once every three months for three times. We will address the following hypotheses

- Is there an influence of the stage of liver disease and alcohol craving on leptin plasma levels and its regulation through methylation?
- Is leptin expression and regulation different in ALD relapsers compared to abstainers?
- Are psychometry scores higher in relapsers compared with abstainers?
- Are psychometry scores positively associated with craving?

Results: In a pilot study, we observed lower leptin levels after LTX when compared to the values found before LTX without obtaining psychometric data. (3)
Conclusion: No strict and binding guidelines exist concerning psychiatric assessment of ALD patients eligible for LTX. We believe that a prospective study on a representative number of patients would allow us to deduce meaningful selection criteria and help to identify the patients who are at a higher risk to show lower therapy adherence or relapse.
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PV077 PILL REDUCTION OF CALCINEURIN INHIBITORS TO IMPROVE MEDICATION ADHERENCE AFTER HEART TRANSPLANTATION

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Introduction: The number of daily pills is shown to be crucial for medical adherence of patients after heart transplantation (HTx) to improve long-term outcome. In this study we identified two methods to reduce the daily count of tacrolimus (TAC) and cyclosporine (CsA): substitution of innovator-TAC with generic-TAC, which offer various dosages, and simplification and systematic adjustment of CsA intake.
Methods: A retrospective study of the immunosuppressive therapy and post-transplant routine examination was conducted on all the patients who received a HTx. The daily dosage was recorded and the daily pill amount was counted. In a theoretic model innovator-TAC was replaced by generic drug, which is available with five different dosages, with the same daily TAC-dosage. For ideal CsA-dosing, we established 2 Models, namely model A, with systematic and targeted adjustment of partial CsA-dosages but keeping the same cumulative daily dose, and model B, with lowest daily pill count by allowing the change of cumulative daily dose within 5%. Then we compared the daily pill amount and costs over the study period.
Results: The average innovator-TAC dosage was 4.8 $\pm$ 3.3 mg/day, and the daily innovator-TAC pill count was 4.1 $\pm$ 1.7. The replacement of innovator-TAC by generic-TAC could lead to a 20.8% volume reduction of TAC pills. The number of TAC pills would be significantly decreased to an average of 3.3 $\pm$ 1.1 mg/day ($p < 0.001$). Furthermore, an annually cost reduction of 19.2% (528 193.01€) could be achieved. The average CsA dosage was 148.9 $\pm$ 42.6 mg/day; the daily pill count was 4.3 $\pm$ 1.1. Using model A, a 28% reduction of daily pill intake could be achieved. Allowing an average change of the cumulative daily dose of 0.6 $\pm$ 2.0% (model B) could result in a 45% reduction of daily pill-count of CsA.
Conclusion: In this study we were able to show that the replacement of innovator-TAC by generic TAC with multiple available dosages, as well as the simplification and systematic adjustment of CsA dosing could significantly reduce the daily pill count, and even the total amount of cost. The reduction of the daily pills could, therefore, increase medication adherence and help to improve outcome after HTx.