TRANSPLANT
INTERNATIONAL

# LECTURES

## KIDNEY

### V01 PRETRANSPLANT DSA BUT NOT COMPLEMENT FIXING HLA ANTIBODIES ARE ASSOCIATED WITH INCREASED RISK FOR ANTIBODY MEDIATED REJECTION IN KIDNEY TRANSPLANTATION

*U. Eisenberger*[1], *D. Keles*[2], *A. Heinold*[2], *O. Witzke*[1], *A. Kribben*[1], *A. Paul*[3], *H.A. Baba*[4], *J.U. Becker*[5], *P.A. Horn*[2], **F.M. Heinemann*[2]

[1]*Klinik für Nephrologie, Universitätsklinikum Essen, Essen, Germany;* [2]*Institut für Transfusionsmedizin, Universitätsklinikum Essen, Essen, Germany;* [3]*Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Universitätsklinikum Essen, Essen, Germany;* [4]*Institut für Pathologie und Neuropathologie, Universitätsklinikum Essen, Essen, Germany;* [5]*Institut für Pathologie, Medizinische Hochschule Hannover, Hannover, Germany*

It is still not fully elucidated whether kidney transplant recipients with preformed donor-specific human leukocyte antigen (HLA) antibodies (DSA) detectable by Luminex Single Antigen Beads (SAB) are at increased risk of reduced allograft function early after transplantation. Especially the effect of complement fixing DSA detected by the C1q SAB assay remains unclear. Regarding the C1q assay recent studies indicated controversial results, possibly related to centre effects or the size of the patient cohorts analyzed.

The aim of our retrospective analysis was to evaluate the early impact of C1q fixing DSA in a large single centre study. We included a cohort of 255/289 renal transplant recipients transplanted in a short period between January 2011 and December 2012 at the local kidney transplantation program in this analysis. All transplantations were performed with a CDC negative crossmatch. For living donation also flow cytometric crossmatches were performed. The pretransplant HLA antibody status determined by Luminex SAB was not systematically considered for transplant decisions. Indication biopsies performed in more than 50 % of all patients within the first one to two years of follow-up for were analysed for histological signs of antibody mediated rejection (AMR).

Pretransplant SAB DSA were present in 40 patients (25 with anti-HLA-class I, 11 with class II, and 4 with class I+II specificities, respectively). In total 27/255 patients showed signs of AMR, 14 of 215 patients without DSA (5.5%, RR 0.2) compared to 13/40 patients with DSA (32.5%, RR 5.2). The C1q fixing capacity was positive in 6/40 patients with DSA, but only in 1/27 patients with AMR. Follow-up data for graft survival and function are pending.

Although still preliminary, our study could clearly confirm pretransplant Luminex DSA as a significant risk factor for the occurrence of early AMR after renal transplantation. C1q-binding capacity of DSA at the time of transplantation seems to be not predictive for the occurrence of AMR during early follow-up.

### V03 EFFECTS OF TREATMENT OF ASYMPTOMATIC HYPERURICEMIA AFTER RENAL TRANSPLANTATION ON MORTALITY AND GRAFT LOSS

**N. Pagonas*[1], *S. Kor*[2], *F. Seibert*[1], *F. Bauer*[1], *A. Giese*[1], *W. Zidek*[2], *T. Westhoff*[1]

[1]*Ruhr-Universität Bochum, Herne, Germany;* [2]*Charité-Universitätsmedizin, Berlin, Germany*

**Background:** Hyperuricemia is very common after renal transplantation. It is associated with increased risk of cardiovascular events and chronic allograft nephropathy. However, no data exist about any benefit of a medical treatment of asymptomatic hyperuriceamia in patients after renal transplantation.
**Methods:** Adult patients who underwent kidney transplantation at the Charité-Universitätsmedizin Berlin between 1996 and 2011 were retrospectively included in the study. Patients were identified from our outpatient charts and the hospital's electronic database by searching with the keywords: hyperuricemia, allopurinol, benzbromaron. Patients were followed-up for a maximal period of 120 months.
**Results:** Of 503 kidney transplant patients were identified and included in the trial. From these, 211 patients with uric acid >7 mg/dl one month after transplantation (no treatment of hyperuricemia at this time) were considered for further analysis. 126 patients were treated with allopurinol ($n = 61$) or benzbromaron ($n = 65$) and 85 did not receive any of these medications in the follow-up period and served as control group. Baseline characteristics did not differ between groups. In the mean follow-up of 78 $\pm$ 35 months 21 patients of the control group and 12 patient in the treatment group had graft loss and returned to hemodialysis ($P < 0.001$). 17 patients in the control group and 29 patients in the treatment group died during follow-up ($P = 0.49$). The combined endpoint graft loss or death was significant lower in the treatment group, even when adjusted for age, gender and eGFR (estimated Glomerular Filtration Rate) at one month after transplantation. Survival rates did not differ between patients treated with allopurinol or benzbromaron.
**Conclusions:** Renal transplant patients with asymptomatic hyperuricemia defined as an uric acid level >7 mg/dl had a longer overall- and graft-survival when treated with allopurinol or benzbromaron in the current trial. To the best of our knowledge, this retrospective analysis constitutes the first study on the effect of treatment of asymptomatic hyperuricemia on mortality and graft loss.

**THORACIC ORGANS I**

## V04 COMBINED HEART-LIVER TRANSPLANTATIONS WITHIN EUROPE – RESULTS OF A ELTR-WIDE SURVEY

*F. Rauchfuß[1], T. Doenst[2], R. Adam[3], J. Pirenne[4], A.D. Pinna[5], J. Hillingsø[6], K. Boudjema[7], J. Klempnauer[8], N. Heaton[9], H. Lang[10], A. Foss[11], H. Wolters[12], O. Kollmar[13], C. Ducerf[14], J. Lerut[15], C. Letoublon[16], F. Lacaille[17], P. Němec[18], U. Settmacher[1,18]

[1]Klinik für Allgemein-, Viszeral- und Gefäßchirurgie, Universitätsklinik Jena, Jena, Germany; [2]Klinik für Herz- und Thoraxchirurgie, Universitätsklinik Jena, Jena, Germany; [3]European Liver and Intestine Transplant Association (ELITA) and Hepatobiliary Centre, Paris, France; [4]Department of Abdominal Transplant Surgery, University Hospitals Leuven, Leuven, Belgium; [5]General Surgery and Transplant Unit, Alma Mater Studiorum-University of Bologna, Bologna, Italy; [6]Department of Surgical Gastroenterology, Rigshospitalet, Copenhagen, Denmark; [7]Service de Chirurgie Hépatobiliaire et Digestive, Centre Hospitalier Universitaire de Rennes, Rennes, France; [8]Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Medizinische Hochschule Hannover, Hannover, Germany; [9]Institute of Liver Studies, King's College Hospital, London, United Kingdom; [10]Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Universitätsklinik Mainz, Mainz, Germany; [11]Division of Cancer Medicine, Surgery and Transplant, Oslo University Hospital Rikshospitalet, Oslo, Norway; [12]Klinik für Allgemein- und Viszeralchirurgie, Universitätsklinik Münster, Münster, Germany; [13]Klinik für Allgemein-, Viszeral- und Kinderchirurgie, Universitätklinik Göttingen, Göttingen, Germany; [14]Department of Digestive Surgery and Liver Transplantation, Croix-Rousse University Hospital, Lyon, France; [15]Starzl Unit of Abdominal Transplantation, University Hospitals St. Luc, Brussels, Belgium; [16]Department of Digestive and Emergency Surgery, University Hospital Grenoble, Grenoble, France; [17]Department of Pediatric Gastroenterology, Necker-Enfants Malades Hospital, Hepatology, and Nutrition, Paris, France; [18]Centre of Cardiovascular and Transplant Surgery, St Anne's Hospital, Brno, Czech Republic

**Introduction:** Combined heart-liver transplantations (CHLT) are rarely performed procedures. European experiences are limited to occasional case reports or case series. Therefore, we conducted, in close collaboration with the European Liver Transplant Registry (ELTR), a survey to acquire the current status of CHLT within Europe.
**Methods:** The survey included an enquiry for recipient and donor demographics, operation data and follow-up data including the immunosuppressive regime after CHLT. The questionnaires were sent to all centres having performed CHLT, which were registered by the ELTR.
**Results:** We obtained data from 57 CHLT. The 1-year- and 5-year-survival in our cohort is 68.4 and 57.9 %. In most cases (52.6 %), indication for CHLT was familial amyloid polyneuropathy (FAP). The operation mode differed widely, but mostly either implantations of the liver were performed after weaning of the cardiopulmonary bypass and without use of a veno-venous bypass ($n = 14$; 31.1 %) or liver transplantation with the recipients still on cardiopulmonary bypass ($n = 13$; 28.9 %). The time period of cardio-pulmonary bypass time was significantly shorter in patients who were liver transplanted after cardio-pulmonary bypass weaning (121 vs. 240 min, $P < 0.000$). The cardio-pulmonary bypass duration was an outcome determining variable: patients with a fastly weaned bypass had a significant better outcome than patients whose liver transplantation was performed while being on cardio-pulmonary bypass ($P = 0.009$). For immunosuppression, most centres used the usual liver protocol (71.4 %) of their centre, followed by the use of the usual heart protocol (24.5 %).
**Discussion:** This series represents by far the largest European cohort of CHLT recipients. Furthermore, it is the largest series describing the operation technique and the immunosuppressive strategies in CHLT patients. Main indication was familial amyloid polyneuropathy. The duration of the cardiopulmonary bypass played an important role in the survival of the recipient and should be taken in account when planning this procedure.

## V05 THE MUNICH LUNG TRANSPLANT GROUP: WAITING LIST DURING THE FIRST 9 MONTHS OF THE LUNG ALLOCATION SCORE ERA

N. Kneidinger, H. Winter, A. Sisic, G. Preissler, C. Neurohr, S. Czerner, T. Weig, M. Dolch, P. Überfuhr, *R. Schramm

Herzchirurgische Klinik und Poliklinik, Ludwig Maximilian Universität München, München, Germany

The Eurotransplant Foundation introduced the lung allocation score (LAS) in Germany on December 10th, 2011. We analyzed characteristics of the Munich Lung Transplant Group (MLTG) waiting list during the first 9 month after the introduction of the LAS.

A mean number of 39 + 1 patients were constantly listed for lung transplantation and 60 transplants were performed by the MLTG during the observation period. While the majority (42 + 0%) of patients waiting for transplant comprised of chronic obstructive pulmonary disease (COPD)/emphysema patients, only 26% of transplanted patients suffered from COPD/emphysema. Instead, the majority (42%) of transplanted patients suffered from interstitial lung disease. Wainting times did not markedly change in the LAS era. Notably, patients with interstitial lung disease had shorter wainting times when compared to patients suffering from COPD/emphysem and cystic fibrosis, both on the waiting list and at the time of transplant.

The MLTG lung transplant waiting list has not markedly changed during the first 9 months after introduction of the LAS. Our data indicate that the LAS accomodates disease-specific patient statuses well. Although patients with interstitial lung disease are preferably transplanted, the LAS system provides a very reasonable basis to also list and transplant COPD/emphysema patients.

## V06 MODULATION OF IMMUNE-MEDIATORS FROM DONOR LUNGS USING THE ORGAN CARE SYSTEM® – A POTENTIAL MECHANISM FOR IMPROVED OUTCOME

*B. Wiegmann[1], C. Falk[2], B. Müller[2], C. Neudörfl[2], A. Akhdar[2], C. Kühn[1], I. Tudorache[1], M. Avsar[1], A. Haverich[1], G. Warnecke[1]

[1]Herz-, Thorax-, Transplantations- und Gefäßchirurgie, Medizinische Hochschule Hannover, Hannover, Germany; [2]Transplantationsimmunologie, Medizinische Hochschule Hannover, Hannover, Germany

**Objectives:** Release of donor-derived immune mediators (IM), triggering allorecognition and inflammation after transplantation (Tx), may impinge on clinical outcome using warm perfusion of donor lungs (Organ-Care-System®, OCS) or standard cold preservation (SOC). IM were analysed in preservation solutions (PS) and peripheral blood (PB), also clinical outcomes monitored.
**Methods:** IM were quantified in perfusion solutions (PS) and plasma at protein level by multiplex-technology at the end of warm preservation ($n = 12$) or cold storage ($n = 9$) and in PB. Donor and recipient demographics and midterm outcomes were analysed.
**Results:** In PS, concentrations of IL-6, IL-10, IL-16, IFN-g CXCL8, CCL4, Ang-2, PECAM-1 and PDGF-b were significantly higher in OCS than SOC ($P < 0.0001$). Inverse distribution was observed for FGF-b ($P = 0.005$). High concentrations in PS following OCS preservation correlated with lower concentrations of several IM in recipient plasma after Tx. OCS vs. SOC median donor age was 44.5 vs. 46 years. Median recipient age was 54.5 vs. 56 years, underlying diagnoses: idiopathic fibrosis ($n = 6$ vs. $n = 5$), cystic fibrosis ($n = 3$ vs. $n = 2$), idiopathic pulmonary hypertension ($n = 0$ vs. $n = 1$) and emphysema ($n = 3$ vs. $n = 1$). No significant differences of the median cross clamp times (minutes) for the right lung (430 vs. 505) and left lung (568.5 vs. 641) were seen. Shorter median ICU-stay was observed in the OCS group (3585 vs. 3750 min), as well shorter mechanical ventilation times (795 vs. 1051 min). Significantly higher %predicted FEV1 at discharge (FEV1) was seen in the OCS group (71% vs. 55%, $P = 0.04$). PGD-scores were lower at T24 in the OCS group ($P = 0.28$). Six-month-survival was not different in this small cohort. Correlations between Ang-2 as well as IL-6 concentrations and FEV1, mechanical ventilation time, paO2/FiO2 and ICU-stay were identified.
**Conclusion:** IM remained low in PS using SOC probably due to reduced metabolic activity in lung tissue during cold ischemia. During OCS preservation, significantly higher amounts of IM were released into PS which may potentially represent depletion from the organ by accumulation in PS. This 'dialysis' effect was associated with reduced inflammatory conditions in the recipient after Tx which, at least in our still limited experience, had a positive impact on the clinical outcome in the OCS group, in particular a tendency towards shorter mechanical ventilation, ICU-stay and lower PGD-scores and significantly higher early FEV1.

**BASIC SCIENCE I**

## V07 INDUCTION OF AN IMMUNOSUPPRESSIVE MECHANISM BY PRETREATMENT OF RECIPIENTS WITH MITOMYCIN-INCUBATED DONOR BLOOOD CELLS IN A RAT HEART ALLOTRANSPLANT MODEL

*F. Sandra-Petrescu[1], C. Kleist[2], K. Nowak[1], L.E. Becker[3], L.P. Jiga[4], L. Dittmar[2], J. Schnotz[2], G. Opelz[2], P. Terness[2]
[1]Surgical Department, University Medical Centre Mannheim, Mannheim, Germany; [2]Department of Transplantation Immunology, Institute for Immunology, University of Heidelberg, Heidelberg, Germany; [3]Department of Internal Medicine I, Division of Nephrology, University of Heidelberg, Heidelberg, Germany; [4]University Department of Plastic Surgery, Oldenburg Evangelical Hospital, Oldenburg, Germany

**Purpose:** Dendritic cells are immunomodulatory cells that can be transformed into suppressive cells by ex vivo treatment with mitomycin C (MMC). We applied the same treatment to peripheral blood mononuclear cells (PBMCs) or blood, and studied their mechanism of action in a rat heart allograft model.
**Methods/Materials:** Donor blood or PBMCs were incubated with MMC, washed and injected i.v. into recipients prior to heterotopic allogeneic heart transplantation. Further, PBMCs were depleted of monocytes and used in the same way. Grafts were analyzed for infiltrating cells, antibody-mediated and chronic rejection. Recipient PBMCs and spleen cells were characterised by flow cytometry and tested in vivo for their regulatory properties.
**Results:** Of $10^8$ MMC-PBMCs significantly prolonged graft survival (65 $\pm$ 17 vs. 9 $\pm$ 0.3 days in untreated and 7 $\pm$ 1 days in PBMC-pretreated controls). MMC-blood treated animals showed a graft survival of 35 $\pm$ 4 days. Depletion of monocytes from MMC-PBMCs abrogated the graft-prolonging action. Suppression was donor- specific since third-party heart allograft survival showed no prolongation.

Analysis of graft infiltrating cells showed a significant increase of Treg-number in tolerated hearts when compared to naïve and rejected hearts (6.4 $\pm$ 3.8 vs. 0.2 vs. 1.1 $\pm$ 0.6 cells/field). Complement activation significantly decreased seven days after transplantation in comparison to rejected hearts. A non-significant narrowing of the vascular lumen of tolerated grafts was observed.

Tolerant recipients had an increased number of Tregs ($CD4^+CD25^+Foxp3^+$) in their blood (6.1 $\pm$ 1% vs. rejected 5.5 $\pm$ 0.3 %) and spleen (8.3 $\pm$ 1.1 % vs. rejected 6.7 $\pm$ 0.1 %). When adoptively transferred into syngeneic recipients these cells induced immunotolerance in contrast to cells from rejecting animals (PBMCs: 133.7 $\pm$ 100.2 vs. 15.2 $\pm$ 3.2; spleen cells: 120 $\pm$ 80 vs. 8 $\pm$ 1.3 days).
**Conclusion:** A single infusion of MMC-treated donor blood cells prior to transplantation strongly prolongs heart allograft survival. This effect might be mediated by MMC-induced regulatory mechanisms including an increase of Treg-number, and inhibition of antibody-mediated rejection.

## V08 $CD27^{low}$ NK CELLS PROLONG ALLOGRAFT SURVIVAL IN MICE BY CONTROLLING ALLOREACTIVE $CD8^+$ T-CELLS IN A T-BET DEPENDENT MANNER

*M. Lantow, E. Eggenhofer, M. Sabet-Baktach, P. Renner, J. Rovira, G.E. Koehl, H.J. Schlitt, E.K. Geissler, A. Kroemer
Department of Surgery, Experimental Surgery, University Hospital Regensburg, University of Regensburg, Regensburg, Germany

**Aim:** We investigated the role of functionally distinct NK cell subsets in alloimmunity. We hypothesized that the dichotomous role of NK cells in transplantation can be explained by the functional heterogeneity of NK cell subsets.
**Methods:** Since T-bet controls the maturation of NK cells from $CD27^{high}$ NK cells to terminally-differentiated $CD27^{low}$ NK cells, we used $Rag^{-/-}T\text{-}bet^{-/-}$ mice (lack $CD27^{low}$ NK cells) to study the roles of $CD27^{low}$ versus $CD27^{high}$ NK cells in a model of T-cell-mediated allograft rejection under co-stimulatory blockade conditions (MR1 + CTLA4Ig).
**Results:** We found that T-cell-reconstituted $Rag1^{-/-}$ recipients (possessing $CD27^{low}$ NK cells) show significantly prolonged allograft survival (7 days MST) upon co-stimulatory blockade when compared to $Rag1^{-/-}T\text{-}bet^{-/-}$ mice (35 $\pm$ 3.4 versus 28 $\pm$ 1.2 days MST), indicating that $CD27^{low}$ NK cells can promote allograft survival. Critically, $Rag1^{-/-}T\text{-}bet^{-/-}$ recipients had strikingly elevated alloreactive memory $CD8^+$ T-cell responses, as indicated by high $CD8^+IFN\text{-}\gamma^+$ T-cell proliferation (1.4-fold). Furthermore, adoptive transfer experiments of $CD27^{low}$ NK cells into $Rag1^{-/-}T\text{-}bet^{-/-}$ STx recipients confirm that $CD27^{low}$ NK cells directly regulate $CD8^+$ T-cell responses by inhibiting the proliferation of alloreactive $IFN\text{-}\gamma^+CD8^+$ T-cells and controlling the availability of donor-derived-IL-15.
**Conclusion:** In summary, mature $CD27^{low}$ NK cells promote allograft survival under co-stimulatory blockade conditions by regulating alloreactive memory $CD8^+$ T-cell responses.

## V09 STRUCTURAL AND FUNCTIONAL BASIS OF ANGIOTENSIN II AND PATHOGENIC IGG MEDIATED $AT_1R$ ACTIVATION

*D. Postpieszala[1], A. Philippe[1], R. Catar[1], G. Riemekasten[2], D. Dragun[1]
[1]Medizinische Klinik mit Schwerpunkt Nephrologie und internistische Intensivmedizin, Charité-Universitätsmedizin Berlin, Berlin, Germany; [2]Medizinische Klinik mit Schwerpunkt Rheumatologie und Klinische Immunologie, Charité-Universitätsmedizin Berlin, Berlin, Germany

Angiotensin II type 1 ($AT_1R$) receptor signals stimuli provided by its natural ligand angiotensin II (Ang II) and pathogenic IgG antibodies ($AT_1R$-IgG) in severe transplant and autoimmune vasculopathies. $AT_1R$ is well established pharmacologic target for several inverse agonists. Our new findings show differences in strength of activation and signalling effectors between Ang II and $AT_1R$-IgG. Elucidation of mechanisms governing $AT_1R$ activation could have broad clinical relevance in renal and cardiovascular medicine.

To study differences in activation between Ang II and $AT_1R$-IgG, we developed a yeast model where the expression of a single human $AT_1R$ is coupled to yeast's growth response in absence of Histidine. First, the human $AT_1R$ cDNA was cloned in a yeast expression plasmid and expressed in the appropriate strain. $AT_1R$ activation was induced by addition Ang II or $AT_1R$-IgG isolated from patients with associated renal pathology.

Both, Ang II and $AT_1R$-IgG triggered a dose-dependent increase in yeasts' growth. $AT_1R$-IgG stimulation induced stronger and more sustainable activation of the receptor than Ang II. Targeted mutagenesis was performed in order to identify which receptor regions govern the activation. Mutating of one cystein contained in the disulfide bridge connecting first (1ECL) and second extracellular loops (2ECL) of the protein impressively decreased activation in response to $AT_1R$-IgG, yet less to Ang II. Random mutations of 2ECL increased both $AT_1R$-IgG and Ang II mediated yeast growth. Finally, an introduction of point mutations associated with receptor activation stressed that specific amino acid changes in the 2ECL of the $AT_1R$ triggered a highest activation of the receptor irrespective of the nature of the stimulus.

We successfully created a model allowing for structural and functional studies of $AT_1R$ receptor plasticity. They provided us with new insights in similarities and differences of binding of $AT_1R$ agonists. Better understanding of the molecular mechanisms responsible for $AT_1R$ activation holds great potential for enhancing renal and cardiovascular health.

**LIVER**

## V10 ENDOSCOPIC ULTRASOUND FOR THE DIAGNOSIS OF BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION

*A. Hüsing, V. Cicinnati, S. Beckebaum, C. Wilms, M. Maschmeier, H. Schmidt, I. Kabar

*Klinik für Transplantationsmedizin, Universitätsklinikum Münster, Münster, Germany*

**Background:** Biliary complications after liver transplantation (LT) are still common and are an important cause of mortality and morbidity. Until now, endoscopic retrograde cholangiopancreatography (ERCP) has been considered the gold standard for diagnosing such complications. The aim of this study was to evaluate the diagnostic yield and therapeutic impact of endoscopic ultrasound (EUS) in the management of biliary complications after LT.
**Methods:** Thirty-seven liver transplant patients who presented with clinical, biochemical, sonographic and / or histological evidence of biliary complications, and who first received EUS followed by ERCP, were enrolled into this prospective observational study. Subsequently, we evaluated the value of EUS in detecting and classifying biliary complications after LT.
**Results:** Thirty-seven biliary complications were detected in 32 patients. Endoscopic ultrasound showed an overall sensitivity and accuracy of 94.6% each. In cases of biliary cast and ischemic cholangiopathy, EUS was found to be diagnostically superior to ERCP and has had, in these cases, a significant impact on clinical decision-making. However, EUS was less reliable when diagnosing anastomotic strictures.
**Conclusion:** EUS can complement ERCP to improve diagnosis of biliary complications after LT and help guide treatment strategies to address these complications.

## V11 CONTRAST ENHANCED ULTRASOUND CHOLANGIOGRAPHY VIA T-TUBE FOLLOWING LIVER TRANSPLANTATION

*S. Chopra[1], C. Grieser[2], J. Pratschke[1], T. Denecke[2]

[1]*Allgemein-, Visceral- und Transplantationschirurgie, Charité Campus Virchow-Klinikum, Berlin, Germany;* [2]*Klinik für Radiologie, Charité Campus Virchow-Klinikum, Berlin, Germany*

The objective was to evaluate contrast enhanced ultrasound (CEUS) based cholangiography compared to conventional radiography as a reference method in patients after liver transplantation. Contrast agents were administered through T-tubes, which were placed during the operation. Twelve patients with side-to-side choledocho-choledochostomy and standardized intraoperative T-tube placement were investigated on the 5th postoperative day (POD 5) with both techniques. All images were digitally acquired and assessed in consensus by two investigators regarding complete anatomic visualization, depiction of pathology (e.g. delayed contrast outflow, stenosis, leakage) and general image quality. CEUS cholangiography showed comparable results in the detection of biliary pathology and overall image quality. Regarding the visualization of the extrahepatic bile duct CEUS produced limited results in six patients. In conclusion, CEUS cholangiography via T-tube represents a potential bedside test for visualization of intrahepatic bile ducts of transplanted livers; it's diagnostic value remains to be determined in further studies.

## V12 COMPLICATIONS REQUIRING REOPERATION AFFECT THE OUTCOME AFTER LIVER TRANSPLANTATION

*J. Andrassy[1], S. Wolf[1], V. Hoffmann[2], M. Rentsch[1], M. Stangl[1], M. Thomas[1], S. Pratschke[1], L. Frey[3], A. Gerbes[4], B. Meiser[5], M. Angele[1], J. Werner[1], M. Guba[1]

[1]*Chirurgie, Klinikum Grosshadern, LMU, München, Germany;* [2]*IBE, Ludwig-Maximilians-University, Munich, Germany;* [3]*Anesthesiology, Ludwig-Maximilians-University, Munich, Germany;* [4]*MED II, Hepatology-Gastroenterology, Ludwig-Maximilians-University, Munich, Germany;* [5]*Transplant Center, Ludwig-Maximilians-University, Munich, Germany*

**Introduction:** Surgical complications may have not only immediate, but also long term effects on postoperative outcomes. Here, we analyzed the effect of surgical (grade 3b) complications requiring an early reoperation on patients'- and graft survival following liver transplantation.
**Methods:** Graft and patient survival in relation to donor and recipient variables and the need for reoperation for complications of 277 consecutive liver transplants performed from January 2007 to December 2012 were analyzed.
**Results:** Of 277 liver transplants were performed in 252 patients. 47% ($n$ = 118) required a reoperation in the early course after transplantation. Overall patient and graft survival at 1, 2 and 3 years was significantly reduced in patients requiring a reoperation. The major impact was found to be within the first 3 months after transplantation. Kaplan-Meier curves showed a similar course thereafter. In the multivariate analysis the need of reoperation, the MELD-score and the cold ischemia time correlated with the overall survival.
**Conclusion:** These data suggest that surgical complications after liver transplantation have a significant impact especially in the early phase after liver transplantation. Therefore, factors that determine the early postoperative course and surgical complication rates are most critical for the outcomes after liver transplantation.

**PAEDIATRIC TRANSPLANTATION**

## V13 C1Q-FIXING DONOR-SPECIFIC HLA ANTIBODIES AT THE TIME OF KIDNEY TRANSPLANT BIOPSY ASSOCIATE WITH LATE GRAFT FAILURE IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

*A. Fichtner[1], C. Süsal[2], B. Höcker[1], S. Rieger[1], R. Waldherr[3], G. Opelz[2], B. Tönshoff[1]

[1]University Children's Hospital, Heidelberg, Germany; [2]Department of Transplantation Immunology, Institute of Immunology, Heidelberg, Germany; [3]Institute for Clinical Pathology, Heidelberg, Germany

**Purpose:** The role of antibody-mediated rejection (AMR) for late graft failure in pediatric renal transplant (RTx) recipients is poorly defined.
**Methods:** We therefore investigated 54 patients undergoing a late biopsy taken for clinical indications (>1 year post-transplant). Patients were tested for DSA and C1q-fixing DSA using the LABScreen Luminex kit (One Lambda) at the time of biopsy.
**Results:** Of 21/54 (39%) of the tested sera were DSA positive. In 20/21 (95%) patients with DSA the DSA were directed against HLA-class-II-antigens and 8/21 (38%) sera were C1q-fixing DSA positive. The 4-year graft survival post biopsy was significantly inferior in the $DSA^+$ (42%) compared to the $DSA^-$ cohort (89%; $P = 0.002$). Furthermore graft survival for patients with C1q-fixing DSAs (12%) was significantly worse compared to $DSA^-$ ($P < 0.001$) or C1q-negative $DSA^+$ patients (77%, $P = 0.04$). Overall 13 grafts failed: 10/13 (77%) patients were DSA positive, 2/13 (15%) were DSA negative, but C4d positive. Cox regression analysis revealed C1q-fixing DSA (HR 6.5) as a significant risk factor associated with graft loss.
**Conclusions:** In pediatric RTx recipients C1q-fixing DSAs at the time of a late graft biopsy for clinical indication associate with subsequent graft failure. In this cohort as many as 92% of the graft failures could be attributed to AMR.

## V14 EPIDEMIOLOGY OF CYTOMEGALOVIRUS (CMV) INFECTION IN PAEDIATRIC RENAL TRANSPLANTATION AND PROPHYLAXIS WITH (VAL-)GANCICLOVIR: AN ANALYSIS OF THE CERTAIN REGISTRY

*B. Höcker[1], S. Zencke[1], K. Krupka[1], A. Fichtner[1], L. Pape[2], L. Dello Strologo[2], I. Guzzo[2], R. Topaloglu[2], S. König[2], J. König[2], M. Bald[2], N. Webb[2], S. Marks[2], A. Noyan[2], F. Yalcinkaya[2], F. Thiel[2], H. Billing[2], M. Pohl[2], H. Fehrenbach[2], T. Bruckner[2], B. Tönshoff[1]

[1]Zentrum für Kinder- und Jugendmedizin, Heidelberg, Germany; [2]For the Certain Registry, Community, Germany

**Purpose:** Controlled studies on (val-)ganciclovir (VGCV) prophylaxis for CMV prevention in paediatric renal transplantation are lacking.
**Methods:** In the framework of the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) Registry, we hence analysed the efficacy and safety of VGCV prophylaxis according to a standardised protocol among 242 paediatric kidney allograft recipients on a CNI-based regimen. 99 patients received VGCV for 3 months post-transplant (prophylaxis group), 143 patients without VGCV serving as controls.
**Results:** CMV high-risk (D+/R-) patients in the prophylaxis group experienced significantly less CMV events (infections and/or diseases) (12/48, 25%) than controls (10/15, 67%, $P = 0.003$). VGCV was generally well tolerated, but associated with a higher rate of anaemia (18% *vs.* 8% in controls; $P = 0.023$), leukopenia (23% *vs.* 10%; $P = 0.002$) and agranulocytosis (13% *vs.* 1%, $P = 0.001$). Patients suffering CMV events had a significantly lower eGFR than CMV-free patients, both 2 years and 3 years post-transplant (54.7 $\pm$ 20.3 vs. 66.4 $\pm$ 21.6 ml/min·1.73 m$^2$; $P = 0.014$).
**Conclusions:** This is the largest study on the efficacy and safety of VGCV in this patient population. VGCV prophylaxis is effective against CMV in paediatric CMV high-risk renal transplant recipients with an acceptable safety profile. CMV infections are associated with a by 17% decreased graft function 3 years post-transplant.

## V15 ABDOMINAL CLOSURE USING AN INTERIM MESH IN SIZE-MISMATCH PEDIATRIC LIVER TRANSPLANTATION – TECHNIQUE DESCRIPTION AND OUTCOME ANALYSIS

*U. Herden, E. Grabhorn, A. Briem-Richter, B. Nashan, L. Fischer

Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany

**Introduction:** Based on a lack of size matched donors most children undergoing liver transplantation (LTX) receive a technical variant graft from adult donors, resulting in a large-for-size situation especially in smaller children. To avoid complications of further graft reduction (e.g. monosegmental LTX) or complications of an oversized liver graft (e.g. reduced graft perfusion, elevated intraabdominal pressure) we use an interim mesh. Here we describe our technique of step wise abdominal closure by a silastic mesh.
**Methods:** Retrospective analysis of our prospective LTX database with review of all surgical reports from 2003–2012. Transplantations were divided based on primary abdominal closure versus usage of a silastic mesh.
**Results:** Overall 298 pediatric LTX were performed, thereof 23 LTX were excluded from the study (1 intraoperative death; 22 combined liver-kidney transplantations). Primary closure was possible after 187/275(68%) LTX, whereas after 88/275(32%) LTX closure was performed using a patch. Decision about usage and size oft the patch (size trimmed) was guided by doppler ultrasound (DU) (single investigator; DU after reperfusion and abdominal closure, guided by systolic peak flow, resistance index, maximum portal flow). DU-guided operative reduction of the patch was performed every 3–4 days. Successful patch removal with definitive closure could be achieved in all children after a median of two revisions (range 1–14), after median 6 days (range 1–67 days) with no abdominal hernia development long-term (median follow-up 89 month). Children with patch were significantly younger 0.7(0–14.9) versus 2.8(0–15.9)years and lighter 7(2–35) versus 12(3–62)kg and had higher GRWR 4.4(1–12.5) versus 2.8(0.7–12)% compared to children with primary closure (all $P < 0.001$). Comparing donor age, weight, height, graft weight or kind of graft there was no significant difference. There was no significant difference in the graft (1-/5-y 78.3/71.5% versus 86.2/68.4%) or patient survival (1-/5-y 94.6/90.5% versus 95.1/90%) between children with or without patch ($P = 0.449/1$).
**Conclusion:** Successful abdominal closure in pediatric LTX using a silastic mesh with step-wise reduction could be achieved without further graft modifying surgery even in children with very large-for-size grafts.

**KIDNEY/PANCREAS I**

## V16 ACTIVATION OF TRANSIENT RECEPTOR POTENTIAL VANILLOID TYPE 1 CHANNELS BY N-OCTANOYL DOPAMINE IMPROVES RENAL FUNCTION AFTER WARM ISCHEMIA BUT NOT AFTER PROLONGED COLD PRESERVATION

*S. Klotz, P. Pallavi, B.K. Krämer, B.A. Yard, S. Hoeger
*Vth medical clinic, University Medical Centre Mannheim, Heidelberg University, Mannheim, Germany*

**Aim:** N-octanoyl dopamine (NOD) improves renal function, when applied shortly before induction of acute kidney injury (AKI). It remains to be assessed how NOD convey its renoprotective properties, if NOD also protects after AKI induction, and if renal allograft recipients also benefit from NOD treatment.
**Methods:** AKI was induced by clamping the left renal artery (45 min) in unilateral nephrectomized Lewis or Spaque Dawley (SD), wild type (WT) and TRPV1$^{-/-}$ rats. Transplantations were performed in the Fisher to Lewis model using a standardized cold ischemia time of 20 h. Treatment was installed directly after restoration of organ perfusion. Renal function, histology and perfusion were assessed by serum creatinine, microscopy and magnetic resonance imaging (MRI) using arterial spin labeling (ASL).
**Results:** NOD significantly improved renal function in AKI WT Lewis and SD rats, but not in TRPV1$^{-/-}$ SD rats. Improved renal function was paralleled by reduced renal inflammation, yet no differences were found in the expression of inflammatory mediators (adhesion molecules and cytokines). Although MRI-ASL, showed a significant lower cortical perfusion in ischemic as compared to non-ischemic kidneys, no influence of NOD was observed. Even though prolonged cold storage did not abrogate TRPV1 activation by NOD, treatment of renal allograft recipients did not show a salutary effect.
**Conclusions:** While NOD treatment improves renal function after warm ischemia induced AKI, it does not so after prolonged cold ischemia. Since the renoprotective effect of NOD depends on TRPV1 activation, it remains to be assessed why its salutary effect is lost after prolonged cold ischemia.

## V17 AGE-RELATED CHANGES IN RAT DONOR KIDNEYS RELEVANT FOR ORGAN QUALITY AND FUNCTION

*A. Fuchs[1], K. Eidenschink[1], S. Wurm[1], W. Gronwald[2], C. Bollheimer[3], B. Banas[1], *M. Banas[1]*
*[1]Abteilung für Nephrologie, Regensburg, Germany; [2]Institut für funktionelle Genomik, Regensburg, Germany; [3]Institut für Biomedizin des Alterns, Erlangen, Germany*

**Background:** Since the need of deceased donor kidneys for transplantation is much higher than organs available, the acceptance of allografts retrieved from older donors in or beyond their seventh decade has been markedly increased. Higher donor age is known to be associated with reduced allograft survival. However, acceptance of elder organs is not standardized yet since the underlying processes in physiological organ aging are not known so far.
**Methods:** Using a well-defined rat model we were interested to analyze functional and histomorphological changes in aging kidneys, age-dependent regulation of the TGF system (as key player of fibrosis), of Toll-like receptors (TLR, as part of the innate immune system) and of chemokines (as prototypic signaling molecules). Furthermore we were interested to find age-specific markers in the urine by NMR-spectroscopy.
**Results:** 3 and 24 months old male Sprague Dawley rats were investigated. Comparing rats 3 months of age with 24 months old rats no changes in blood pressure and heart rate could be detected. Old rats showed significantly increased proteinuria. Computer-aided morphometry of glomeruli demonstrated significantly increased accumulation of matrix, collagen and desmin, a marker for podocyte damage, in old rat kidneys. KI 67 staining revealed a significantly reduced cell proliferation in older rat kidneys. Electron microscopy confirmed structural changes of glomerular cells, membranes and matrix. TGFß1, TGFß2, Smad2, CCL5 and most TLR investigated (except TLR2,3 and 9) showed a significant higher mRNA expression in 24 months old rat kidneys. The numbers of T cells present in peritubular and periglomerular compartments and around vessels were much higher in older rats. Using NMR spectroscopy significant differences could be seen for 6 of the analyzed metabolites.
**Conclusion:** Healthy 24 months old rat kidneys show significant structural changes compared to younger kidneys. Locally expressed markers of fibrosis and immune activation were associated with kidney aging and infiltration of immune cells was observed. Regarding these results increasing knowledge about kidney aging will lead to novel methods and biomarkers for classifying pre-transplant organ quality. An adequate selection, combination and dosing of immunosuppressive drugs should help to increase the long-term function of allografts accepted from donors with advanced biological age.

## V18 COMPLEMENT RECEPTOR (C5AR & C5L2) DEFICIENCY IN ACUTE KIDNEY INJURY (AKI)

*R. Chen[1], *A. Thorenz[1], S. Rong[1], B. Hensen[2], M. Meier[3], D. Hartung[2], P. Dutow[4], H. Haller[1], K. Hüper[2], A. Klos[4], F. Güler[1]*
*[1]Klinik für Nieren- und Hochdruckerkrankungen, Medizinische Hochschule Hannover, Hannover, Germany; [2]Diagnostische Radiologie, MHH, Hannover, Germany; [3]Imaging Center ZTL, MHH, Hannover, Germany; [4]Microbiology, MHH, Hannover, Germany*

**Background:** Acute kidney injury (AKI) and is a relevant complication after in solid organ transplantation: incidence after lung tx: ~50–75 % and 40–70% after liver tx. AKI increases early post-operative morbidity and mortality. Rapid activation of the complement cascade with binding of C5a to C5aR and the orphan receptor C5a like 2 (C5L2) mediates inflammation and modulates the innate and adaptive immune response. So far, little is known about the differences between the C5aR and the C5L2 receptor mediated downstream signaling in ischemia reperfusion injury (IRI).
**Methods:** AKI by ischemia reperfusion injury (IRI) was induced in C5aR and C5L2 deficient and wild type control mice (WT; C57Bl/6) by transient unilateral clipping of the right renal pedicle for 45 min. The renal morphology, the glomerular filtration rate (GFR), renal blood flow (RBF) and expression of pro-fibrotic and pro-inflammatory markers and infiltrating leukocytes were analyzed three weeks after injury induction. Functional magnetic resonance imaging (MRI) was performed to further analyze renal perfusion and kidney volume.
**Results:** Complement receptor deficiency attenuated inflammation and macrophage infiltration due to IRI. In addition, fibrosis and collagen deposition were attenuated compared to WT mice. The protective effects in C5L2 deficient mice were clearly more pronounced than in C5aR deficient mice. By functional MRI we could show that IRI caused severe impairment of renal perfusion with a maximum at d7 and only little recovery after 3 weeks. In addition WT mice showed severe kidney volume loss correlating with progressive renal fibrosis. C5L2 deficient mice had a similar impairment of renal perfusion at d1 but less further decrease towards d7 and totally recovered to normal renal perfusion at 3 weeks. In line with the better renal perfusion, kidney volume loss was significantly less in C5L2 deficient mice at 3 weeks after IRI.
**Conclusion:** The study points towards a distinct role of C5L2 and C5aR signalling in inflammation and AKI. Complement modulating therapies might be promising therapeutic targets in treatment of AKI and also delayed graft function.

## V19 ASSOCIATIONS OF SMOKING WITH ALTERATIONS IN RENAL HEMODYNAMICS MAY DEPEND ON SEX – INVESTIGATIONS IN POTENTIAL KIDNEY DONORS

*H. Guberina[1], M. Baumann[1,2], H. Bruck[3], T. Feldkamp[4], J. Nürnberger[5], A. Kribben[1], T. Philipp[1], O. Witzke[1], G. Sotiropoulos[6], A. Mitchell[1]*
*[1]Klinik für Nephrologie, Universitätsklinikum Essen, Essen, Germany; [2]Abteilung f. Nephrologie, II. Medizinische Klinik und Poliklinik, Klinikum rechts der Isar, München, Germany; [3]Medizinische Klinik III, Helios Klinikum, Krefeld, Germany; [4]Klinik f. Nieren- und Hochdruckkrankheiten, Innere Medizin IV, Universitätsklinikum Schleswig Holstein, Kiel, Germany; [5]Klinik f. Nephrologie und Dialyse, Helios Klinikum, Schwerin, Germany; [6]Klinik f. Allgemeinchirurgie, Viszeral- und Transplantationschirurgie, Universitätsklinikum Essen, Essen, Germany*

**Problem:** Cigarette smoking is a risk factor for renal damage, but little is known about subclinical effects of smoking on renal hemodynamics and parameters of renal function in humans. We examined the associations of smoking with systemic and renal hemodynamics and renal function parameters in healthy individuals.
**Methods:** Data from 196 potential living kidney donors were analysed retrospectively. Mean arterial blood pressure (MAP), effective renal plasma flow (ERPF) and creatinine clearance had been measured. We additionally calculated parameters of renal hemodynamics. Data were analyzed for the effects of smoking and sex dependent on age and MAP.
**Results:** Systemic and renal hemodynamic parameters did not differ between smokers and non-smokers. In non-smokers of both sexes MAP was negatively correlated with ERPF, and higher MAP was associated with increased renal vascular resistance and afferent arteriolar resistance, with glomerular pressure ($P_G$) remaining constant. However, in male, but not in female smokers, ERPF and $P_G$ increased with MAP. A correlation of age with a steeper decline in ERPF in male smokers was lost in multiple regression analysis.
**Conclusions:** As compared to women, smoking men may exhibit an increased glomerular hydrostatic pressure, which is a known promoter of kidney damage.

## V20 CORRELATION BETWEEN GLOMERULAR FILTRATION RATE (GFR) AND DIFFERENT MOLECULAR FORMS OF PSA

*K. Fischer, G. Theil, K. Weigand, P. Fornara
Universitätsklinik und Poliklinik für Urologie und Nierentransplantationszentrum, Halle/Saale, Germany

**Introduction:** In patients with kidney insufficiency serological cancer markers should be interpreted with caution, because some markers are affected by reduced renal elimination. Several studies showed there is no significant effect of terminal renal failure on total PSA (t-PSA). This is different from free PSA (f-PSA): renal insufficiency leads to increased serum levels of this low molecular weight PSA form and causes a shift of the f/t-PSA ratio to higher values. Little data exists concerning the behaviour of complexed PSA (c-PSA) under the conditions of renal failure.
**Materials and Methods:** Blood samples have been analyzed for t-PSA, f-PSA and c-PSA in 104 patients (37 dialysis patients, 29 after renal transplantation and 38 with normal renal function). The correlation to the GFR (according to MDRD formula) was calculated. There is no significant difference in regards to age and prostate volume between the study groups. There are statistically significant differences between the GFR of the three patient groups ($P < 0.000$).
**Results:** The GFR has no influence on the serum values of t-PSA and c-PSA (correlation coefficients according to Pearson, 0.009 respectively 0.017). In contrast, f/t-PSA ratio is negatively correlated with renal function (correlation coefficient according to Pearson −0.415).
**Conclusion:** It seems that t-PSA and c-PSA are not affected by renal function. The ratio f/t-PSA shifts with decreasing GFR to higher values. Therefore, the decision limit of f/t-PSA ratio of men with normal kidney function is non-applicable to men with reduced GFR. Especially in transplant recipients the renal function should be taken into account when interpreting the f/t-PSA.

## V21 DURATION OF IN HOUSE MACHINE PERFUSION AFTER COLD STORAGE AND ITS IMPACT ON EARLY REPERFUSION PARAMETERS IN PORCINE KIDNEYS

*A. Gallinat[1], P. Effertz[2], A. Paul[1], T. Minor[2]
[1]Universitätsklinikum, Essen, Germany; [2]Universitätsklinikum, Bonn, Germany

**Background:** In house machine perfusion after cold storage (hypothermic reconditioning) has been proposed as convenient tool to improve kidney graft function. The present study aimed to investigate the influence of the duration of machine perfusion for early reperfusion parameters in porcine kidneys.
**Methods:** Kidney function after cold preservation (4°C, 18 h) and subsequent reconditioning by one or 4 h of pulsatile machine perfusion (HMP) was studied in an isolated kidney perfusion model in pigs ($n = 6$, resp.) and compared with simply cold stored grafts (CS).
**Results:** Compared to CS alone, 1 h of subsequent HMP significantly reduced perfusate concentrations of endothelin-1 and increased vascular release of nitric oxide upon warm reperfusion. Renal flow and kidney function (clearance and sodium reabsorption) were also significantly improved. The beneficial effect of HMP was not altered by extension of the HMP time to 4 h. Molecular effects of HMP comprised a significant (vs CS) mRNA elevation of the endothelial transcription factor KLF2 along with significantly lower expression of endothelin that were observed already at the end of 1 h HMP after CS.
**Conclusion:** Reconditioning of cold stored kidneys is possible, even if clinical logistics allow for as little as 1 h of therapy, while limited extension of the overall cold storage time by in house machine perfusion might also allow for postponing of the transplantation from night to early day work.

**THORACIC ORGANS II**

## V22 MIDTERM CLINICAL OUTCOME IN HEART TRANSPLANT RECIPIENTS RECEIVING THYMOGLOBIN FOR INDUCTION THERAPY

*U. Fuchs, A. Zittermann, S. Ensminger, A. Amini, U. Schulz, J. Gummert
*Thorax – und Kardiovaskularchirurgie, HDZ NRW, Bad Oeynhausen, Germany*

We have recently presented data showing that heart transplant recipients who require induction therapy with thymoglobin (THY) have a higher 1-year mortality than heart transplant recipients with standard therapy, especially when those patients were major histocompatibility complex (MHC) antibody positive. Here we present data on midterm mortality in HTx patients receiving calcineurin inhibitor-free induction therapy. We followed for up to five years a group of 55 patients who received THY (39 MHC positive patients and 16 patients with chronic kidney disease stages III-IV) and a control group ($n = 55$) who received standard immunosuppressive therapy. Age, sex, and diagnosis were comparable between the two groups ($P > 0.05$), whereas body mass index was significantly higher in the THY group compared with the control group (26.4 $\pm$ 3.8 kg/m$^2$ vs. 24.1 $\pm$ 4.1 kg/m$^2$; $P = 0.006$). Median follow up was 43.1 months (IQR:5.0–50.4 months) in the THY group and 45.6 months (IQR:36.8–51.7 months) in the controls. Unadjusted mortality tended to be higher in the THY group compared with the controls (34.5% vs. 18.2%; $P = 0.051$). However, the multivariable-adjusted hazard ratio (HR) of mortality did not differ between groups (HR for the THY group=1.69 (95%CI:0.78–3.68; $P = 0.187$). In the surviving patients, postoperative CRP levels remained longer elevated and postoperative platelets and white blood cell counts showed a more pronounced transient decrease in the THY group compared with the controls ($P = 0.001$–$0.046$). Compared with HTx patients receiving standard immunosuppressive therapy, our data indicate an acceptable midterm survival in the group of high-risk patients who require CNI-free induction therapy.

## V23 CLINICAL OUTCOME IN HEART TRANSPLANT RECIPIENTS RECEIVING EVEROLIMUS PLUS DOSAGE REDUCTION OF TACROLIMUS

*U. Fuchs, A. Zittermann, S. Ensminger, M. Wasgien, U. Schulz, J. Gummert
*Thorax – und Kardiovaskularchirurgie, HDZ NRW, Bad Oeynhausen, Germany*

It is currently not known whether in heart transplant (HTx) recipients the combination of everolimus (EVL) plus dosage reduction of tacrolimus (TAC) is superior to the regular TAC dosage regimen regarding clinical outcomes. We compared 5-year survival and kidney function in 67 maintenance HTx patients receiving EVL plus dosage reduction of TAC (EVL group) with 67 patients matched for age, sex and transplantation date receiving the regular TAC regimen (TAC group). Statistical analyses were performed using Kaplan-Meier survival estimates and 2-factor ANOVA. Initial estimated glomerular filtration rate (eGFR) was significantly lower and blood leucocyte counts were significantly higher in the EVL group compared with the TAC group (GFR: 38.5 $\pm$ 13.2 vs. 67.3 $\pm$ 29.5 ml/min/1.73$^2$;respectively, $P < 0.001$, blood leucocyte counts: 8.4 $\pm$ 2.9 vs. 7.0 $\pm$ 2.110$^9$/l, respectively, $P = 0.002$). Five-year mortality did not differ between groups (19.4% vs. 17.9%; $P = 0.766$). There were however significant time x treatment effects with respect to eGFR values ($P < 0.001$). In detail, eGFR decreased on average by 10 ml/min/1.73 m$^2$ during follow up in the TAC group but increased by 8 ml/min/1.73 m$^2$ in the EVL group. Blood leucocyte counts improved significantly in the EVL group but not in the TAC group ($P = 0.008$). Parameters of liver function did not change significantly, either in the EVL group or in the TAC group. EVL plus dosage reduction of TAC improved kidney function compared with the regular TAC dosage regimen. Despite poorer initial kidney function and higher blood leucocyte counts in the EVL group, 5-year survival was comparable between the two groups.

## V24 INFLUENCE OF MITRAL REGURGITATION AT TIME OF IMPLANTATION ON OUTCOME IN PATIENTS WITH VENTRICULAR ASSIST DEVICES

*A. Bernhardt, K. Muellerleile, M. Barten, D. Biermann, F.M. Wagner, H. Reichenspurner, T. Deuse
*Universitäres Herzzentrum Hamburg, Hamburg, Germany*

**Objectives:** Mitral regurgitation (MR) of any degree is a common finding in failing hearts and often due to left ventricular dilatation. However, the impact of MR at the time of left ventricular assist device (LVAD) implantation on outcome still remains unclear. The aim of this study was to evaluate changes in left ventricular geometry and MR grade during follow-up and the influence of pre-implant MR on long-term outcome.
**Methods:** Thirty-five consecutive patients, mean age 57.6 $\pm$ 11.5 years, underwent HeartWare HVAD implantation without concomitant mitral valve repair. Mean follow-up was 9.9 $\pm$ 7.1 months. Prospectively compiled trans-thoracic echocardiography data (baseline and follow-up) were retrospectively analyzed. Endpoints were death, stroke, thrombembolism, major bleeding and right heart failure during follow-up. Follow-up was complete in all patients.
**Results:** Left ventricular (LV) enddiastolic diameter decreased from 73.61 $\pm$ 12.13 mm to 64.36 $\pm$ 13.04 mm ($P = 0.04$). At the time of implantation, 27 patients (77.1%) had MR of any degree and in 17 patients (48.6%), MR was graded moderate to severe. At 3 months follow-up, only one patient (2.8%) had moderate MR and 12 patients had mild MR (34.3%); thus, the degree of MR decreased in a significant portion of patients. One-year survival in patients without MR at implant was 80% compared to 52% in patients with moderate to severe MR ($P = 0.156$). One-year event-free survival was 72% in patients without MR vs. 33% in patients with moderate to severe MR ($P = 0.035$).
**Conclusions:** The LV diameters and MR grades decreased during LVAD support. Although survival was not significantly different, event-free survival was significantly more common in patients that did not present moderate to severe MR at time of LVAD implantation.

## V25 THE USE OF ROUTINE ENDOMYOCARDIAL BIOPSY FOR DIAGNOSIS OF CELLULAR REJECTION BEYOND 2 YEARS AFTER CARDIAC TRANSPLANTATION

*C. Heim, M. Weyand, R. Tandler
*Herzchirugrie, Universität Erlangen-Nürnberg, Erlangen, Germany*

**Introduction:** Endomyocardial biopsy (EMB) is widely used for routine surveillance of cardiac allograft rejection. The need for continued EMB beyond the first year after cardiac transplantation is controversial. EMB is performed through the jugular or femoral veins and is associated with a complication rate of less than 1%. The aim of this study was to investigate the use of EMB in monitoring long term surviving heart transplant recipients.
**Methods:** We conducted a retrospective chart review of all patients at our center 2 years or more after heart transplantation.97 long-term survivors after HTx between 2000 and 2011 were included in this study. Significant cellular rejection was defined as grade 2R or 3R using ISHLT nomenclature. Patients were analyzed assessing immunosuppressive regimen and procedural related complications.
**Results:** Out of 97 long-term survivors of cardiac transplantation, 17 patients developed at least 1 episode of significant late (>2 years after Tx) cellular rejection (17.5%). Analyzing the respective immunosuppressive regimen showed increased number of calcineurin inhibitor (CNI)-free regimen (64.7%) in patients rejecting late after heart transplantation. Only 35.3% of late cellular rejections occurred in patients treated with Ciclosporin A or Tacrolimus. The overall incidence of procedural related complications was low (1.0%) and none was life threatening.
**Conclusion:** The above data demonstrates that endomyocardial biopsies continue to detect clinically significant rejection beyond 2 years after cardiac transplantation. Late rejection was not depending on previous episodes of early cellular rejections. Therefore, we recommend routine endomyocardial biopsies in cardiac transplant recipients even though late after transplantation.

## V26 CLOPIDOGREL PRESERVES MICROVASCULAR VASCULAR INTEGRITY IN ORTHOTOPIC TRACHEAL TRANSPLANTS AFFECTED BY OBLITERATIVE BRONCHIOLITIS

*C. Heim[1], M.A. Khan[2], B. Motsch[1], S. Müller[1], T. Stamminger[1], M.R. Nicolls[2], M. Weyand[1], S. Ensminger[1,3]

[1]Herzchirugrie, Universität Erlangen-Nürnberg, Erlangen, Germany; [2]Stanford University School of Medicine, Palo Alto, CA, USA; [3]HDZ NRW, Bad Oeynhausen, Germany

**Introduction:** Survival after lung transplantation is mainly limited by the development of chronic lung allograft dysfunction (CLAD). The aim of this study was to investigate if platelet inhibition by clopidogrel has an influence on the microvascular integrity of orthotopic tracheal allografts and the formation of obliterative bronchiolitis, present in the majority of patients suffering from CLAD.
**Methods:** C57Bl/6 ($H2^b$) donor tracheas were orthotopically transplanted into CBA.J ($H2^k$) recipients. Mice received clopidogrel alone or in combination with everolimus. Grafts were analyzed by serial tissue PO2 monitoring by a fluorescence quenching technique. Blood flow monitoring was performed by laser Doppler flowmetry and a Lectin-binding assay to analyze the function of the microvasculature on postoperative days 4, 10 and 30.
**Results:** Isografts showed a stable tissue PO2 and blood flow during the initial timepoints after transplantations. In contrast, allografts showed a steady decline in tissue PO2 and blood flow in rejecting airway allografts until the PO2 nadirs 10–12 days after transplantation. Continous administration of clopidogrel (Clopi) or Everolimus (Evero) alone and in combination (EC) significantly improved tissue oxygenation, limited microvascular leakiness, and prevented airway ischemia. (Fig. 1)
**Conclusions:** These data demonstrate that clopidogrel alone and in combination with everolimus ameliorates microvascular injury during acute airway rejection and subsequently reduces post-transplant obliterative bronchiolitis.

## V27 HVAD CONTINUOUS FLOW VENTRICULAR ASSIST DEVICE FOR ISCHEMIC VENTRICULAR SEPTAL RUPTURE – NO NEED FOR A TOTAL ARTIFICIAL HEART!

*A. Bernhardt, H. Reichenspurner, T. Deuse

Universitäres Herzzentrum Hamburg, Hamburg, Germany

**Background:** Ventricular septal defect after myocardial infarction (post-MI-VSD) is a severe complication and associated with high mortality. Surgical closure is necessary for all hemodynamically-relevant shunts, but surgery has a high risk of postoperative right or left heart failure. Total artificial heart implantation is a classical indication for patients in cardiogenic shock from post-MI-VSD.
**Methods:** Three patients with post-MI-VSD (age 46, 47 and 67 years old) emergently underwent HeartWare ventricular assist devices (HVAD) implantation. The patients were in INTERMACS class 1 to 2. In two patients, an occluded LAD was the reason for acute LV failure and the post-MI-VSD. The patients had surgical patch closure of the VSD with concomitant LVAD implantation. In these patients, the VSD patch was extended around the LV apex like a modified Dor plasty and had the HeartWare sewing ring attached to it. In another patient, an occluded RCA led to post-MI-VSD and caused predominant RV failure. He had VSD patch closure and the HVAD was implanted into the RV. Procedural and clinical outcomes were analysed.
**Results:** All three patients survived the first 30 days and could be discharged. The first patient had an uneventful follow-up of six months. The second patient had a pump thrombosis of the RVAD and the device was explanted with partially recovered RV function after 3 months. Due to a recurrence of RV failure, however, the patient required heart transplanted six months later and recovered completely. The third patient died of a fatal device mishandling six months after LVAD implantation.
**Conclusion:** Surgical closure of post-MI-VSD with concomitant continuous flow LVAD or RVAD implantation is feasible and might obviate the need for a total artificial heart in these specific patients.

**BASIC SCIENCE II**

## V28 COSTIMULATION BLOCKADE BY BELATACEPT INHIBITS ALLO-SPECIFIC DE NOVO T CELL RESPONSES AND PRESERVES VIRUS-SPECIFIC MEMORY T CELL RESPONSES IN HEALTHY DONORS AND KIDNEY TRANSPLANTED PATIENTS

*C. Neudörfl[1], K. Daemen[1], M. Stevanovic-Meyer[1], J. Keil[1], U. Hoffmann[1], F. Lehner[2], H. Haller[3], C. Blume[3], W. Hammerschmidt[4], R. Zeidler[4], *C.S. Falk[1]*

*[1]Institut für Transplantationsimmunologie, IFB-TX, MHH, Hannover, Germany; [2]Abteilung Abdminal und Transplantationschirurgie, MHH, Hannover, Germany; [3]Abteilung Nieren- und Stoffwechselerkrankungen, MHH, Hannover, Germany; [4]AGV Genvektoren, HMGU, München, Germany*

**Purpose:** Belatacept (Bela) inhibits T cell activation at the interaction between costimulatory CD28 and its ligands CD80/CD86. Side effects are minimal compared to calcineurin or mTOR inhibitors. However, patients with Belatacept-based immunosuppression showed increased acute T cell mediated rejections (TCMRs) early after kidney transplantation (KTx) and more frequently EBV or CMV reactivation. EBV-derived virus like particles (VLPs) are currently discussed as vaccination strategy for Ktx candidates. Our project was designed to compare inhibitory capacities of Bela, CNI, mTORi regarding allogeneic de novo and memory virus-specific T cell responses in healthy donors and kidney recipients.
**Methods:** IFNg-ELISpots and intracellular cytokine staining were performed with PBMCs of healthy donors (HD) ($n = 9$) or KTx patients ($n = 7$) with or without Bela, CTLA-4-Ig or CNI/mTORi. Supernatants were tested for cytokines by multiplex assays. T cells were stimulated with CMV, EBV or flu peptides (CEF), allogeneic LCL, EBV-VLPs or PHA as control. Binding of Bela to CD80/CD86$^+$ immune cells was compared to CTLA-4-Ig.
**Results:** While CNI completely blocked both virus- and allospecific T cell responses, Bela was unable to inhibit virus-specific IFNg production of memory T cells. In contrast, IFNg and IL-2 but not IL-10 and IL-17 production by de novo allo-specific T cells was inhibited by Bela and CTLA-4-Ig in HD and KTx patients. Bela displayed stronger binding than CTLA-4-Ig to CD80/CD86 + immune cells. Compared to CNI, mTORi were less efficient in inhibiting T cell responses. EBV-VLPs induced weak IFNg production in CD4 + T cells in HD whereas significantly weaker responses were seen in KTx patients.
**Conclusions:** In contrast to CNI, virus-specific memory T cell responses were not impaired in HD and kidney Tx patients by costimulation blockade. Allo-specific IFN-g and IL-2 production was impaired by costimulation blockade while other cytokines remained unaffected which may be responsible for the increased TCMR frequency early after KTx. EBV-specific VLPs may represent vaccination strategy for KTx patients despite their limited capacity to induce T cell responses. Our studies argue for individual variability of the sensitivity towards Bela among HD and KTx recipients which implies that predisposition of the immune response determines susceptibility to costimulation blockade.

## V29 COSTIMULATORY BLOCKADE SUPPRESSES TH1- BUT NOT TH2- AND TH17-MEDIATED ALLOIMMUNE RESPONSES

*M. Sabet-Baktach[1], E. Eggenhofer[1], P. Renner[1], M. Lantow[1], J. Rovira[2], H.J. Schlitt[1], E.K. Geissler[1], A. Krömer[1]*

*[1]Klinik und Poliklinik für Chirurgie, Uniklinik Regensburg, Regensburg, Germany; [2]Department of Nephrology and Renal Transplantation, Hospital Clinic Barcelona, Barcelona, Spain*

**Background:** Costimulatory blockade resistant allograft rejection remains an understudied obstacle of this promising strategy for tolerance induction in transplantation. Therefore, the purpose of this study was to evaluate the responsiveness of distinct T helper cell subsets to treatment with costimulatory blockade.
**Methods:** We transferred purified T cells from B6.RORγt knockout (KO), B6.T-bet KO, and B6.RORγt-T-bet double KO (DKO) mice into B6.Rag-common-γc DKO recipients of fully mismatched Balb/c skin allografts +/- treatment with CTLA4Ig and anti-CD154.
**Results:** Untreated controls from all used mouse strains promptly rejected their skin allografts with similar kinetics. However, immunological analyses (histology, flow cytometry, ELISA) revealed that RORγt KO T cell recipients showed a Th1-mediated allograft rejection while T-bet KO recipients featured a Th17/Th2-driven rejection. Moreover, DKO T cells rejected early with a Th2 phenotype (high IL-4 levels and eosinophilic allograft infiltration). Importantly, under treatment with costimulatory blockade RORγt KO T cells showed a significantly prolonged allograft survival (MST 76.2 days+/−24.3 days), whereas T-bet KO (MST 22.25 days+/−8.5 days) or DKO recipients rejected promptly (MST 27.5 days+/−10.1 days) with a mixed Th2/Th17 and Th2 phenotype, respectively (as indicated by IL4, IL-17 and IFN-γ levels in FACS and ELISA).
**Conclusion:** These results indicate that costimulatory blockade differentially affects Th2 and Th17 versus Th1 alloresponses, resulting in allograft rejection.

## V30 ACUTE REJECTION IN MURINE RENAL TRANSPLANTATION IS ALLEVIATED BY A NOVEL INHIBITOR OF THE MCP1/CCR2 SIGNALING PATHWAY

*A. Kalnins[1], M. Notohamiprodjo[2], S. Müller[3], M. Thomas[1], M. Rentsch[1], M. Stangl[1], A. Habicht[4], B. Meiser[4], M. Fischereder[5], J. Werner[1], M. Guba[1], K. Nicolaou[2], J. Andrassy[1]*

*[1]Chirurgie, Klinikum Grosshadern, LMU, München, Germany; [2]Radiology, University of Tuebingen, Tuebingen, Germany; [3]Pathology, Ludwig-Maximilians-University, Munich, Germany; [4]Transplant Center, Ludwig-Maximilians-University, Munich, Germany; [5]MED V, Internal Medicine – Nephrology, Ludwig-Maximilians-University, Munich, Germany*

**Introduction:** Biopsies are often required to detect acute rejection after renal transplantation. Here, we tested a novel substance which inhibits the MCP1/CCR2 pathway via oligonucleotides in a murine renal Tx model. The aim was 1.) to detect potential effects of this drug on acute rejection processes and 2.) show that new imaging techniques may be helpful for a non-invasive monitoring.
**Methods:** Kidneys of Balb/c mice were transplanted onto B6. Mice were either treated with the anti-MCP1-Spiegelmer in monotherapy or in combination with subtherapeutic CsA (10 mg/kgBW). Transplant function was assessed by MRI on d 10. The outcome was compared with results from histology, immunohistochemistry, doppler ultrasound and RT-PCR.
**Results:** The number of F4/80$^+$ cells was significantly suppressed and kidney cortex perfusion measurements improved under combination therapy. IFN-g and TNFa were significantly suppressed under mono- and combination therapy. Similar results were found for BAFF. The apparent diffusion coefficient (ADC) of native kidneys and syngenic allografts did not show significant differences. Allogenic allografts without treatment showed significantly lower ADC ($P < 0.001$). Under combination therapy the ADC significantly improved ($P = 0.002$).
**Conclusion:** The novel drug based on oligonucleotide technology inhibiting the MCP1 alleviates acute rejection especially as an adjunct. Diffusion-weighted MRI may serve as new tool to non-invasively detect rejection processes.

## V31 ISOLATED TRANSFER OF HUMAN PLATELETS RESULTS IN FORMATION OF TRANSPLANT ARTERIOSCLEROSIS IN A RAG2$^{-/-}$γ-CHAIN$^{-/-}$ MOUSE AORTIC XENOGRAFT MODEL

*C. Heim[1], S. Müller[1], B. Weigmann[2], A. Gocht[1], B. Motsch[1], M. Ramsperger-Gleixner[1], R. Zimmermann[2], M. Weyand[1], S. Ensminger[1,3]*

*[1]Herzchirugrie, Universität Erlangen-Nürnberg, Erlangen, Germany; [2]Universität Erlangen-Nürnberg, Erlangen, Germany; [3]HDZ NRW, Bad Oeynhausen, Germany*

**Background:** Platelets play an important role in the formation of vascular lesions. The aim of this study was to investigate the interaction of isolated human platelets (hPlts) with human endothelium in a Rag2$^{-/-}$γc$^{-/-}$ mouse model of human arterial xenotransplantation.
**Methods:** Inactivated and TRAP6-stimulated hPlts were phenotyped for surface markers (CD62p,CD63) by flow cytometry. Recovery of 2'–7'-dichlorofluorescein-labeled hPlts was detected with an in vivo fluorescence imager and by flow cytometry. Side branches of human mammary artery were implanted into the infrarenal aorta of Rag2$^{-/-}$γc$^{-/-}$ recipients, followed by daily application of $4 \times 10^8$ inactivated or activated hPlts. Arterial grafts were analyzed by histology on day 30 after transplantation.
**Results:** Inactivated hPlts showed low levels of CD62p and CD63 [17.32 ± 2.20% / 3.75 ± 0.84% ($n = 6$)]. After TRAP6 stimulation (activated hPlts), expression of CD62p and CD63 was markedly increased [89.03 ± 3.70% / 79.79 ± 4.13% ($n = 6$, $P < 0.001$)]. Circulating DCF-labeled hPlts were detected within the lung, liver, kidney, spleen and arteries of recipients. Activated platelets had lower in vivo recoveries compared to inactivated platelets after 60 min [4.53 ± 0.32%/36.71 ± 3.04% ($n = 5$, $P < 0.001$)]. Daily intravenous injection of inactivated or activated hPlts both groups showed intimal proliferation 30 days after transplantation [Rag2$^{-/-}$γc$^{-/-}$ + inactivated hPlts: 59.37 ± 4.91% ($n = 5$, $P < 0.001$ vs. control) and Rag2$^{-/-}$γc$^{-/-}$ + activated hPlts: 70.42 ± 19.55% ($n = 3$)].
**Conclusion:** Here we can show that isolated application of inactivated or activated hPlts in the absence of T-, B- and NK-cells results in the significant amounts of transplant arteriosclerosis.

## V32 OPTIMISATION OF HEPATOCYTE TRANSPLANTATION USING REGULATORY T CELLS – AN *IN VITRO* MODEL USING PRIMARY HUMAN HEPATOCYTES

*D. DeTemple[1], M. Kleine[1], C. Falk[2,3], W. Ramackers[1], M. Jaeger[1], J. Klempnauer[1], H. Bektas[1], F.W.R. Vondran[1,3]

[1]AG ReMediES, Allgemein-, Viszeral- und Transplantationschirurgie, Medizinische Hochschule Hannover, Hannover, Germany; [2]Institute of Transplant Immunology, Integrated Research and Treatment Centre Transplantation, Medizinische Hochschule Hannover, Hannover, Germany; [3]German Centre for Infection Research, Hannover-Braunschweig, Germany

**Background:** The liver is generally considered an immunoprivileged organ with comparatively low risk of rejection regarding solid organ transplantation. In accordance with this, tolerant liver transplanted patients show a higher percentage of regulatory T cells ($T_{reg}$) within the grafts. As key players of tolerance, they are capable of suppressing T cell mediated immune responses, but also may regulate effectors of innate immunity. Concerning human hepatocytes, only limited data is available on immunological processes involved following cell transplantation. Hence, this project's objectives were characterisation of hepatocyte-induced T cell responses as well as evaluation of the immunomodulatory potential of $T_{reg}$ in this setting.

**Methods:** Hepatocyte isolation was carried out in a 2-step perfusion technique from partially resected livers and then cultured as monolayers. $T_{reg}$ were sorted for a $CD4^+CD25^{high}$ phenotype from human peripheral blood lymphocytes and expanded with CD3/CD28-expanderbeads and high doses of interleukin-2. Using flow-cytometry, cell proliferation in mixed lymphocyte cultures (MLC) and mixed lymphocyte hepatocyte cultures (MLHC) was detected by labelling responder cells with PKH-26. Furthermore, multi-colour flow-cytometry was applied for characterisation of T cell subpopulations. Cytokine profiles from culture supernatants were determined by Bio-Plex technology.

**Results:** In comparison to conventional MLC, the T cell response to allogeneic stimulation with hepatocytes (MLHC) was distinctly reduced and showed a delayed onset. The reaction appeared to be especially $CD4^+$ T cell mediated, whereas the $CD8^+$ -subpopulation only proliferated slightly. However, an early up-regulation of the CD69-expression could be observed in this subgroup. T cell activation was efficiently suppressed by adding $T_{reg}$, whose immunomodulatory effect could be verified not only in the proliferative response but also in the cytokine profiles.

**Conclusion:** Primary human hepatocytes induce an especially $CD4^+$ T cell mediated immune response when co-cultured with allogeneic lymphocytes. Regulatory T cells have shown a promising potential for the modulation of these immune reactions.

**LIVER/SMALL INTESTINE**

## V34 OPERATIONAL TOLERANCE CAUSES A LONG LASTING ACTIVE IMMUNOREGULATION WITHIN THE GRAFT

*R. Taubert[1], R. Danger[2], M.-C. Londono[3], M. Martinez[3], A. Rimola[2], M.P. Manns[1], A. Sanchez-Fueyo[2,3], *E. Jaeckel[1]*

*[1]Gastroenterologie, Hepatologie & Endokrinologie, Medizinische Hochschule Hannover, Hannover, Germany; [2]Institute of liver studies, King's College Hospital, London, UK; [3]Liver Unit, Hospital Clinic Barcelona, Barcelona, Spain*

**Aims:** Immunosuppression (IS) can be discontinued from selected, stable patients after liver transplantation resulting in operational tolerance (OT). While biomarkers can predict the outcome of IS withdrawal, the mechanisms mediating OT remain elusive.
**Methods:** In the current study, we analyzed serial liver biopsies obtained from adult liver recipients enrolled in a prospective multi-center IS withdrawal trial employing immunophenotyping and transcriptional profiling. Liver samples were collected before the initiation of IS withdrawal, at the time of rejection, or 1 and 3 years after complete drug discontinuation. In parallel immune cells from peripheral blood were analysed by flow analysis.
**Results:** Out of the 102 recipients participating in the trial, IS withdrawal was successful in 41 recipients. We analyzed mechanisms of tolerance in 15 patients with serial biopsies. The number of liver infiltrating T cell subsets did not differ at baseline between patients who rejected and those who successfully discontinued IS, However, to our surprise the tolerated grafts exhibited portal tract expansion with increased T cell infiltration despite normal transaminases and no signs of rejection one year after IS withdrawal. This was associated with preferential accumulation of CD4 + Foxp3 + T cells, a shift in the CD4/CD8 T cell ratio and a trend towards up-regulation of immune activation and regulatory genes. At three years after induction of operational tolerance the grafts had still large inflammatory infiltrates, but with reduced CD8 + T cells leading to an increased CD4/CD8 ratio suggestive of additional deletional mechanisms. The inflammatory gene signature returned to baseline 3 years after IS withdrawal. Changes within the graft were not paralleled by analysis of PBMCs.
**Conclusion:** We report here for the first time data suggesting that in human liver transplant recipients OT is an active, long-lasting phenomenon in which IS withdrawal elicits dominant immunoregulatory mechanisms that restrain effector alloimmune responses. The results will need to be taken into account when designing future diagnostic and therapeutic clinical studies aiming at achieving allograft tolerance in clinical organ transplantation.

## V35 TUMOR DNA-INDEX AND α-FETOPROTEIN LEVEL DEFINE OUTCOME FOLLOWING LIVER TRANSPLANTATION FOR ADVANCED HEPATOCELLULAR CARCINOMA

**A. Andreou, G. Puhl, A. Pascher, M. Bahra, P. Neuhaus, J. Pratschke, D. Seehofer*

*Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Campus Virchow-Klinikum, Charité, Berlin, Germany*

**Background:** Patients with hepatocellular carcinoma (HCC) beyond the Milan criteria (MC) are expected to have an inferior outcome after liver transplantation (LT) and are therefore currently not considered for LT in many countries. The purpose of this study was to identify predictive factors for overall survival (OS) following LT for HCC that may support MC in the selection of appropriate transplant candidates.
**Patients and Methods:** Clinicopathological data of 364 patients with HCC who underwent LT in a high-volume transplant center between 1989 and 2010 were retrospectively evaluated. Predictors of overall survival in the entire cohort as well as in subsets of patients within ($n$ = 214) and beyond ($n$ = 150) the MC were analyzed.
**Results:** After a median follow-up time of 78 months the median survival (MS) was 100 months. Factors associated with OS in univariate analysis included recipient age, tumor DNA-index, α-fetoprotein level (AFP), MC, bilobar lesions, microvascular invasion, tumor differentiation, and hepatitis C. In multivariate analysis, DNA-index>1.5 ($P < 0.0001$), AFP>200 ng/ml ($P = 0.009$), and HCC beyond MC ($P = 0.003$) independently predicted worse OS. In patients within the MC (MS = 170 months), DNA-index>1.5 ($P < 0.0001$) was the only predictive factor for OS in multivariate analysis. In patients beyond the MC (MS = 44 months), DNA-index>1.5, AFP>200 ng/ml, microvascular invasion, patient age > 60 years and DNA-index>1.5 concomitant with AFP>200 ng/ml were associated with worse OS in univariate analysis. Multivariate analysis identified DNA-index>1.5 concomitant with AFP>200 ng/ml ($P < 0.0001$) as the only independent predictor of worse OS.
**Conclusions:** DNA-index and AFP level predict OS following LT in patients with advanced HCC beyond the MC. Combined assessment of these markers during the evaluation of transplant candidates can contribute to the selection of patients with HCC who may benefit from LT independently of their tumor burden.

## V36 REEVALUATION OF RATS' HEPATIC VASCULAR ANATOMY – GETTING READY FOR ALLPS MODEL

**W. Wei[1], A. Schenk[2], C. Sänger[1], O. Dirsch[1,3], U. Settmacher[1], U. Dahmen[1]*

*[1]Department of General, Visceral and Vascular Surgery, Jena University Hospital, Jena, Germany; [2]Liver Research, Fraunhofer MEVIS, Bremen, Germany; [3]Institute of Pathology, Jena University Hospital, Jena, Germany*

**Background:** Associating Liver Partition with Portal Vein Ligation for Staged Hepatectomy (ALPPS) is a surgical strategy which induces a rapid regeneration of the future liver remnant (FLR). Regeneration seems to be faster than after classical PVL. However, the underlying mechanism is not yet investigated. Therefore we did a detailed anatomical study to clarify the anatomy of the portal vein and median hepatic vein of rats as a prerequisite to develop a surgical model.
**Method:** Reevaluation of the detailed vascular anatomy of ML was performed. 10 explanted livers were subjected to imaging techniques after microfil injection. 3D reconstruction was performed in order to visualize the spatial distribution of the vascular branches of portal vein and hepatic vein.
**Result:** Similar to the human liver, the ML was supplied by the right median and left median portal branches (RMPB and LMPB) and the parallel hepatic arterial branches. The ML was drained by 3 main branches: right median, middle median and left median hepatic vein (RMHV, MMHV and LMHV). The main bifurcation of MMHV was located in RML, draining not only the middle portion of ML, but also the anterior portion of LML. However, the spatial distribution of the branching pattern was subject to some variations potentially influencing the size of the territory at risk of outflow obstruction.
**Conclusion:** According to our anatomical study, it seems better to perform transection along the umbilical fissure in rats, although it can cause outflow obstruction of anterior portion of LML. In this case, a resection of the anterior portion of LML could be discussed.

## V37 PREDICTIVE VALUE OF EARLY POSTOPERATIVE MELD SCORES ON PATIENT AND GRAFT SURVIVAL AFTER LIVER TRANSPLANTATION

**A. Khandoga, E. Iskandarov, M. Rentsch, M. Stangl, M. Angele, J. Werner, M. Guba*

*Klinik für Allgemeine, Viszeral-, Transplantations-, Gefäß- und Thoraxchirurgie, Ludwig-Maximilians-Universität München, München, Germany*

Early allograft dysfunction after liver transplantation is not well defined. The aim of this study was to evaluate predictive value of early postoperative MELD scores on 3- and 12-months survival.

In this single center retrospective study, 362 consecutive patients after liver transplantation were included. MELD scores at 7, 14, and 21 postoperative days (POD) were calculated from primary lab values.

About 89% of patients survived 3 months and 84% one year after transplantation. The graft survival rate was 84% after 3 months and 69% after one year. The MELD scores were on POD-7 21 ± 7 and 18 ± 8 (dead vs. alive patients, respectively), on POD-14: 20 ± 8 vs. 15 ± 7, at POD-21: 19 ± 8 vs. 15 ± 7 As shown by ROC analysis, the best cutoff of MELD score predicting the one-year patient survival was on POD-14 (17 for one-year survival and 19 for 3 months-survival, p

In conclusion, MELD scores early after liver transplantation are predictive for 3 and 12 months outcome. The postoperative MELD score on POD-14 is a good predictor for the patient survival and on POD-7 for the graft survival after liver transplantation.

## V38 DEVELOPMENT OF A MODEL FOR ESTIMATION OF SUBCUTANEOUS HEPATITIS B IMMUNOGLOBULIN DOSE REQUIREMENT AFTER LIVER TRANSPLANTATION

*S. Beckebaum, A. Hüsing, I. Kabar, G. Wu, H. Schmidt, V.R. Cicinnati

*Klinik für Transplantationsmedizin, Universitätsklinikum Münster, Münster, Germany*

Subcutaneous HBIG dosing according to summary of product characteristics (SPC) which is based solely on a cutoff value of 75 kg body weight to categorize patients in those requiring a single (<75 kg, 500 IU/week) or a double shot (≥75 kg, 1000 IU/week) may not be sufficient to reliably estimate HBIG requirement. High interindividual variability of anti-HBs consumption may be of multifactorial etiology including distinct HBIG distribution and clearance. In our HBV transplant study, we aimed to identify predictive parameters for sc HBIG consumption. Laboratory parameters and bioelectrical impedance analysis were determined over 12 months from liver transplant (LT) HBV recipients ($n = 43$) who were converted from 2–3 monthly iv HBIG± nucleos (t) ide analogues (NUC) to weekly sc HBIG±NUC to identify additional factors that may impact anti-HBs titers. Pearson correlation analysis showed that anti-HBs titers were negatively associated with estimated glomerular filtration rate, total protein, total body water, fat-free mass and muscle mass and positively associated with serum creatinine, body weight, body mass index, body waist and fat mass. These results suggest that body composition may impact HBIG levels through distinct HBIG distribution. For a drug eliminated primarily via renal excretory mechanisms, renal dysfunction may also alter pharmacokinetics and pharmacodynamics. Moreover, we developed a model including "easy-to-apply" predictors for HBIG dose requirement that avoids excess titers and reduces the economic burden of passive immunoprophylaxis.

**HOT TOPICS**

## V39 ORGAN ALLOCATION: CAN WE JUSTIFY THE PRIORITY GIVEN TO CHILDREN?

*M. Bobbert
*Institut für Geschichte und Ethik der Medizin, Medizinische Fakultät, Heidelberg, Germany*

In Germany as well as in the whole Eurotransplant region organ allocation rules give priority to children. Paediatricians refer to impending developmental disorders, and thus to the ethical principle of prevention of harm. They hereby imply that the medical urgency of adult patients has not the same ethical importance. Opponents of this priority rule argue that adults should not be discriminated against and all patients be given equal opportunity of their life being saved. Moreover, opponents object that in times of extreme organ shortage for example women of small height and weight do not have the chance to get a liver transplant. Rather, they have to accept a split-liver which involves several disadvantages in regard to complication and success rates.

Strong moral intuitions militate in favour of children's priority. At first sight, deontological theories seem to claim equality of chance and respect of dignity of every human being, regardless of their age or stage of life. Several promising arguments in favor of such a prioritization will be discussed, for example the idea to allow children a "normal life-span" or the idea of strengthening children as beings with no blame in the causation of their organ failure.

## V40 CHINA'S ORGAN HARVESTING FROM PRISONERS: A NEVER ENDING STORY?

*H. Li
*Institut für Pharmakologie, Universitätsmedizin Mainz, Mainz, Germany*

Medical organizations worldwide condemn the use of organs from executed prisoners. China is the only country in the world that still systematically takes organs from executed prisoners for transplantation. Recently, Chinese officials announced the plan to integrate organs from executed prisoners into the public voluntary organ donation and allocation system. Huang Jiefu, director of the China Organ Donation Committee and former vice-minister of health, told Beijing Times on March 04 that "once the organs from willing death-row prisoners are enrolled into our unified allocation system, they are then counted as voluntary donation from citizens; the so called death-row donation doesn't exist any longer." If this plan is accepted by the international community, China will continue using prisoner organs and the unethical practice would officially bypass international standards. In addition to the acknowledged organ source of executed prisoners, there is accumulating evidence that China also harvests organs from political prisoners without consent. A recent piece of evidence came from the case of Wang Lijun, former police chief of Jinzhou City, who referred to several thousand cases in his transplantation research from 2004 to 2006. Transplantation professionals in the world must respond actively to stop this barbaric practice immediately.

## V41 VALIDATION OF THE SUITABILITY OF LOPHIUS BIOSCIENCES T-TRACK® CMV TO ASSESS THE FUNCTIONALITY OF CELL-MEDIATED IMMUNITY (CMI) IN HEMODIALYSIS PATIENTS

B. Banas[1], C. Böger[1], G. Lückhoff[2], B. Krüger[1], *A. Starke[3], H. Bendfeldt[3], J. Batzilla[3], M. Schemmerer[3], J. Köstler[4], S. Barabas[3], R. Wagner[3,4], L. Deml[3], J. Leicht[5], B.K. Krämer[6]
[1]*Department of Internal Medicine II, University Medical Center Regensburg, Regensburg, Germany;* [2]*Dialysis Center Landshut, Landshut, Germany;* [3]*Lophius Biosciences GmbH, Regensburg, Germany;* [4]*Institute for Medical Microbiology and Hygiene, University Regensburg, Regensburg, Germany;* [5]*Dialysis Center Schwandorf, Schwandorf, Germany;* [6]*5th Department of Medicine, University Medical Center Mannheim, Medical Faculty Mannheim of the University of Heidelberg, Mannheim, Germany*

**Objective:** Impairment of cytomegalovirus (CMV)- specific cell-mediated immunity (CMI) by immunosuppressive therapy is a major cause for CMV reactivations and associated complications in solid organ transplantation. Thus, assessing the function ofCMV- specific CMI may help to predict the onset of complications and to individually adjust immunosuppressive as well as antiviral therapy. The novel diagnostic tool T-Track® CMV allows the simultaneous detection of CMV- reactive T-helper- and cytotoxic T-cells as well as NK- and NKT-cells using *activated* pp65 and IE-1 proteins for *in-vitro* restimulation of PBMC and a highly standardized IFN-gELISpot assay. The aim of this cross sectional multicenter study was to evaluate the suitability of the novel tool T-Track® CMV for assessing the functionality of CMV-specific CMI in a clinically relevant pre-transplant patient population.
**Methods:** Test sensitivity and specificity of T-Track® CMV were examined in a cohort of 124 hemodialysis patients of whom 67 (54%) revealed a CMV positive serostatus. Moreover the results of T-Track® CMV were compared with Quantiferon®-CMV and a cocktailof 6 preselected CMV tetramers as reference tests.
**Results:** Positive T-Track® CMV results were obtained in 60/67 (sensitivity 89.6%) of CMV- seropositive hemodialysis patients. Low, however significant numbers of IE-1- but not pp65- reactive cellswere observed in12 of 57 CMV-seronegative dialysis patients confirming data from other groups showing IE-1 specific T-cell responses in seronegative individuals.

For comparison, the reference tests Quantiferon®-CMV and CMV tetramer cocktail revealed sensitivities of 72.6% (45/62) and 76.9% (40/52), respectively.
**Conclusion:** T-Track® CMV can be used in a broad population of hemodialysis patients independent of their HLA-type. Thus, T-Track® CMV assay may also represent a valuable tool to assess functionality of CMV-specific CMI in transplant recipients and help to guide personalized antiviral and immunosuppressive therapy.

**PSYCHOSOMATICS**

## V44 FREQUENCY OF SYMPTOMS OF DEPRESSION AND ANXIETY IN DIALYSIS AND LIVER CIRRHOSIS PATIENTS BEFORE AND AFTER ADMISSION TO THE WAITING LIST

*R.M. Heeb[1], G. Greif-Higer[2], I. Krämer[1]
[1]Department of Pharmacy, Johannes-Gutenberg-University Medical Center, Mainz, Germany; [2]Department of Psychosomatic Medicine and Psychotherapie, Johannes-Gutenberg-University Medical Center, Mainz, Germany

**Introduction:** Symptoms of depression and anxiety are known in patients with end stage kidney or liver disease who are potential candidates for organ transplantation. The aim of this study was to evaluate the frequency of symptoms of depression and anxiety in transplant candidates before and after admission to the waiting list.
**Methods:** Patients on dialysis or suffering from liver cirrhosis were evaluated by the Hospital Anxiety and Depression Scale (HADS) questionnaire. Results were stratified according to the underlying disease and age (<60; ≥60 years).
**Results:** In total, 41 dialysis and 42 liver cirrhosis patients were evaluated. In patients ≥60 years, 45% of the dialysis and 27% of liver cirrhosis patients and in patients <60 years, 25% of dialysis and 57% of liver cirrhosis patients indicated symptoms of depression. Symptoms of anxiety were observed in 30% of the dialysis patients, independent from age. In liver cirrhosis patients 52% of patients <60 years and 36%of patients ≥60 years showed symptoms of anxiety.
**Conclusion:** Patients with chronic liver and kidney disease show significant differences in the frequency of symptoms of depression or anxiety depending on the type of disease and age. These results have to be further analyzed in the context of quality of life and medication adherence.

## V45 DELISTING AND "INACTIVE STATUS": SURVEY ON ETHICAL ASPECTS OF MANAGING A WAITING LIST IN TIMES OF DECREASING ORGAN DONATION

*R. Viebahn, P. Kühn, A. Wunsch, P. Schenker
Chirurgie, Knappschaftskrankenhaus UK RUB, Bochum, Germany

The German „transplant scandal" had a severe impact on all aspects of organ transplantation in Germany. Mainly the donor rates dropped by almost 30% causing longer waiting times and an increase of death on the waiting list. The cause of manipulation in German liver transplant programs may have been the fact that only patients with a MELD>35 were transplanted with the consequence of accelerated postoperative morbidity and mortality. Thus the question of access to and removal from the waiting list has to be discussed: Should patients inappropriate for transplantation be listed and should patients be delisted after getting too sick for transplantation?

By surveying „google" (g) and „pubmed" (p) the dimension of discussion was quantified. Subsequently the retrieved articles on pubmed were analyzed concerning the decision criteria and their coverage of ethical dimensions.

The following number of hits was retrieved: „delisting and kidney transplantation": g: 104.000, p:3, „delisting and cardiac transplantation": g:21.900, P:15, „delisting and liver transplantation": G:1.150.000, p: 15, „delisting and lung transplantation": g:41.100, p:4. Almost every publication retrieved in p gave clear cut medical criteria for listing and delisting, however delisting was ony a small chapter. Only three publications touched ethical aspects. Several papers compared the prognosis after delisting with remaining on the list and transplantation. Delisting does not seem to have a definite beneficial effect on the waiting list as well as the consequences of „inactivating" a candidate. In heart transplant programs patients may be delisted because they recovered by medical treatment and became „too good for transplantation".

The high number of retrievals in google demonstrates that delisting and inactivating are of great interest in the waiting list management of liver transplantation. Obviously the guidelines in the other fields of transplantation are clear enough. The ethical aspects of „adequacy for transplantation" remain poorly assessed.

## V46 WHICH RULES FOR ORGAN DONATION AND ALLOCATION ARE ETHICALLY ACCEPTABLE AND EFFECTIVE IN RELIEVING THE SHORTAGE OF TRANPLANTABLE ORGANS?

*R. Osterkamp
Economics, Bavarian School of Public Policy, Bichl, Germany

**Objectives:** The paper aims at defining formal and informal rules of organ donation and allocation which are politically and ethically acceptable and would contribute to relieving the global shortage of transplantable organs.
**Material and Methods:** 1. The literature of medical, health economics and ethics on organ shortage is assessed with respect to existing and possible new rules for organ donation and allocation.

2. 80 empirical surveys in rich and poor countries on the preference of people for alternative rules of organ donation and allocation are assessed.
**Results:** The literature shows that reciprocity rules would contribute to relieving the organ shortage. From empirical surveys one can conclude that many people consider a system of organ donation and allocation as a fair system if it is based on reciprocity. The paper shows how reciprocity rules could be implemented in national and international legislation on organ donation and allocation.
**Conclusions:** The national and global shortage of transplantable organs leads transplant physicians and politicians to reconsider the current rules of organ donation and allocation. Additional elements of reciprocity to the current rules should be a guidepost for further reforms.

**KIDNEY/PANCREAS II**

## V47 DUODENAL LEAKS AFTER PANCREAS TRANSPLANTATION WITH ENTERIC DRAINAGE – CHARACTERISTICS AND RISK FACTORS

*V. Spetzler, N. Goldaracena, M. Marquez, J. Schiff, I. McGilvray, M. Cattral, M. Selzner

*Multi Organ Transplant Unit, Toronto General Hospital, Toronto, ON, Canada*

**Background:** Simultaneous pancreas-kidney (SPK) and pancreas after kidney (PAK) transplantation with enteric drainage has become a standard treatment in diabetic patients with renal failure. Leaks of the graft duodenum are a common complication after transplantation. We studied causes and predisposing factors of duodenal leaks in both SPK and PAK transplantation.
**Method:** Between January 2002 and April 2013 284 pancreas transplantations with enteric drainage were performed at our institution including 191 SPK (67.3%) and 93 PAK (32.7%). We analyzed the occurrence of duodenal leaks, anamnestic risk factors, leak etiology, and graft survival.
**Results:** Out of 18 duodenal leaks (incidence 6.3%), 12 cumulated over the first 100 days after transplantation. 6 pancreas grafts with duodenal leak were rescued by duodenal segment resection. PAK transplantation sequence (odds ratio 3.526, $P = 0.008$) and preoperative immunosuppression (odds ratio 3.328, $P = 0.012$) were significant risk factors for duodenal leaks. In the SPK subgroup, postoperative peak amylase as marker of reperfusion injury was associated with an increased incidence of duodenal leaks. No anamnestic donor or recipient aspect showed a significant influence on duodenal leak occurrence.
**Conclusion:** Long-term immunosuppression in PAK transplantation is a risk factor for duodenal leaks. Early surgical revision offers the chance of pancreatic graft rescue.

## V48 COMPARISON OF HISTIDINE-TRYPTOPHAN-KETOGLUTARATE (HTK) SOLUTION AND UNIVERSITY OF WISCONSIN (UW) SOLUTION IN PANCREAS TRANSPLANTATION

*S. Grzella, R. Viebahn, P. Schenker

*Chirurgische Universitätsklinik, Universitätsklinikum Knappschaftskrankenhaus Bochum, Bochum, Germany*

**Backround:** HTK solution is currently the most common used solution for pancreas transplantation (PT) in Germany. The use of HTK is controversial, particular in pancreas grafts with longer ischemia times.
**Methods:** A total of 240 PT (218 SPK, 16 PAK, 6 PTA) procedures were performed in our centre between 2002 and 2012. HTK was used in 133 patients, and UW in 107 patients. We retrospectively compared our experience with these two types of preservation solutions, focusing on graft and patient survivals, as well as postoperative complications.
**Results:** Demographic data of donors and recipients showed no significant difference.

With a mean follow-up of 75.2 $\pm$ 39.9 months, both groups demonstrated comparable patient survivals after 1, 3 and 5 years (HTK 96.2, 94.7 and 92.0%; UW 95.3, 91.7 and 90.7%, $P = 0.451$). Pancreas graft survival rates after 1.3 and 5 years were significant better in the HTK-group (84.2, 82.6, 80.0%) vs. the UW-group (74.9, 71.1, 67.3%) $P = 0.013$. Relaparotomy-rate within the first three postoperative months was not significant different for both the groups (HTK 44.36% versus UW 43.93%). Serum amylase and lipase values did not differ between both groups.

In a subgroup analysis of 98 pancreas grafts (UW 44 / HTK 54) with a cold ischemic time > 12 h (mean CIT UW: 14.2 $\pm$ 1.7; HTK: 14.1 $\pm$ 1.6) UW and HTK were similar.
**Conclusion:** In our study, we demonstrate equal results for patient survival, and a better pancreas graft survival using HTK in pancreas transplantation. No increased incidence of allograft pancreatitis or graft loss was observed, especially in PT with longer ischemic time. However, this study has some limitations (single center, retrospective), and the comparison of both solutions was an analysis of two different time points as well (UW-group historically older). Therefore, the results should be interpreted with caution.

## V49 ELUCIDATING ISCHEMIA REPERFUSION INJURY IN HUMAN RENAL TRANSPLANTS BY MICRORNA PROFILING USING NEXT GENERATION SEQUENCING

*T. Singer[1], V. Haselmann[2], U. Benck[1], R. Eichner[2], S. Porubsky[3], R. Waldherr[3], M. Neumaier[2], B. Krämer[1], B. Krüger[1]

*[1]V. Medizinische Klinik, Universitätsmedizin Mannheim, Mannheim, Germany; [2]Institut für Klinische Chemie, Universitätsmedizin Mannheim, Mannheim, Germany; [3]Pathologisches Institut, Universitätsmedizin Mannheim, Mannheim, Germany*

Small noncoding RNA fragments of 20–24 bp, so called microRNAs, are important gene regulators in various (patho-) physiological processes. To date, pre-perfusion kidney biopsies fail to predict post-transplant pathologies, especially delayed graft function) as a consequence of ischemia reperfusion injury (I/R-injury). Profiling of microRNA, obtained by next generation sequencing, might offer the ability to generate specific molecular patterns to elucidate pathways in I/R -njury and predicting clinical outcome.

Formalin-fixed paraffin embedded (FFPE) pre perfusion biopsies of different clinical graft injuries were used to perform microRNA profiling. The next generation sequencing platform “Ion Torrent” was used to assess microRNA profiles. Data were analyzed by Geneious Pro

In all biopsies with different clinical graft injuries robust and reproducible microRNA profiles, even if only small amounts of tissue could be used, were obtained. Different microRNA profiles with differential expression could be shown in an unsupervised hierarchical clustering which revealed specific microRNA expression patterns related to clinical outcome and graft injury.

This work proved the ability of microRNA profiles to offer the potential of revealing specific pathways which are involved in graft injury after renal transplantation. Further research is needed to clarify the interaction between specific microRNAs, gene expression, graft injury and clinical outcome.

**INFECTIONS AND COMPLICATIONS**

## V51 HIGH SVR AFTER TELAPREVIR BASED ANTIVIRAL TRIPLE THERAPY FOR HCV-REINFECTION AFTER ORTHOTOPIC LIVER TRANSPLANTATION

*F. Klein, D. Eurich, R. Neuhaus, J. Pratschke, M. Bahra

*Klinik für Allgemein-, Visceral- und Transplantationschirurgie, Charité Campus Virchow, Universitätsmedizin Berlin, Berlin, Germany*

**Background:** The development of graft cirrhosis due to HCV-reinfection remains a major problem after orthotopic liver transplantation (OLT). Protease inhibitors have extended the antiviral treatment options especially in genotype-1 infected HCV relapsers and non-responders to Pegylated Interferon/Ribavirin therapy. The aim of this study was to analyze the significance of telaprevir based triple therapy for patients with HCV-reinfection after OLT.
**Methods:** We included 12 patients with histologically confirmed graft fibrosis due to HCV-reinfection. Treatment duration was scheduled for 12 weeks of telaprevir based antiviral triple therapy followed by 36 weeks of consecutive dual therapy with Pegylated Interferon/Ribavirin.
**Results:** Of 6/12 patients (50%) completed the full 48 weeks of antiviral treatment. Triple therapy had to be discontinued in one patient due to non-response and in one patient due to severe hematological side effects. Four patients did not complete dual therapy due to hematological and/or renal side effects. One year after begin of antiviral treatment 8/12 patients (66%) showed a sustained virological response (SVR).
**Conclusion:** Telaprevir based triple therapy may be an effective treatment option for individual patients with HCV graft hepatitis. However treatment management is complex and patients need to be carefully monitored for drug-drug interactions and possibly severe treatment-related side effects.

## V52 DACLATASVIR, SIMEPREVIR AND RIBAVIRIN AS A NEW IFN-FREE TRIPLE REGIMEN FOR HCV RECURRENCE AFTER LIVER TRANSPLANTATION: FIRST RESULTS OF SAFETY AND EFFICACY IN 6 PATIENTS

*A. Papadopoulos-Köhn[1], J. Timm[2], A. Canbay[1], C. Jochum[1], A. Paul[3], G. Gerken[1], *K. Herzer[3,1]*

*[1]Klinik für Gastroenterologie und Hepatologie, Uniklinikum Essen, Essen, Germany; [2]Institut für Virologie, Universitätsklinikum Essen, Essen, Germany; [3]Allgemein- Viszeral- und Transplantationschirurgie, Uniklinikum Essen, Essen, Germany*

**Background:** Recurrent HCV infection following liver transplantation leads to accelerated allograft injury and is associated with reduced graft and patient survival. Therapeutic intervention with interferon is difficult due to poor efficacy and tolerability. The application of first generation PIs is limited due to drug-drug interactions with immunosuppressants (IS). The introduction of new IFN-free therapeutic options with DAA-combinations are in the prospect to substantially improve the outcome for LT patients with HCV.
**Methods:** Daclatasvir 60 mg/daily, simeprevir 150 mg/daily and ribavirin 600 mg /daily were administered as an all oral triple regimen to 6 LT patients with recurrent HCV infection, one with genotype 1a and 5 with genotype 1b. All patients were treated for 24 weeks and monitored closely concerning trough levels of IS (one received everolimus and five tacrolimus), laboratory parameters and potential side effects.
**Results:** One patient experienced a viral breakthrough at treatment week (tw) 8 which was associated with emergence of resistance-associated mutations in the NS3 protease domain as well as a NS5A deletion. Antiviral regimen was successfully swiched to sofosbuvir / RBV in this case. The remaining five patients cleared viral load between tw 4 and 8 and achieved end of treatment response (EOT), three patients have a SVR4 at that stage. Clinical parameters (ALT, AST, bilirubin, fibrosis stage) improved in all patients except a moderate transient increase of bilirubin in one. All patients tolerated the medication very well. Adverse events were hardly observed and limited to moderate anemia due to RBV. Uptake of IS and trough levels were constant during therapy, the dose of IS did not have to be adjusted.
**Conclusions:** Our observations suggest the described regime as safe and efficient for LT patients and provide great promise for the use of this all-oral antiviral regimen in other immunosuppressed and IFN-intolerant HCV patients.

**ORGAN DONATION/MARGINAL ORGANS**

## V53 BEGGARS CAN'T BE CHOOSERS: THE FATE OF DECLINED LIVER ORGAN OFFERS

*A. Kleespies[1], V. Onnebrink[1], S. Pratschke[1], M. Angele[1], M. Rentsch[1], J. Andrassy[1], G. Denk[2], A. Gerbes[2], M. Kaspar[3], T. Breidenbach[4], B. Meiser[5], J. Werner[1], M. Guba[1]

[1]Department of General-, Visceral-, Transplantation-, Vascular- and Thoracic Surgery, University of Munich, Munich, Germany; [2]Department of Medicine 2, University of Munich, Munich, Germany; [3]Department of Anesthesiology, University of Munich, Munich, Germany; [4]Region Bayern, Deutsche Stiftung Organtransplantation (DSO), Munich, Germany; [5]Transplant Center Munich, University of Munich, Großhadern, Munich, Germany

**Background:** In a scenario of severe organ shortage the decline of potentially transplantable livers has to be critically analyzed. With the intention to evaluate our clinical decision-making within the organ acceptance process, we have followed the fate of liver organ offers, that were declined by our transplant team.
**Methods:** Declined organ offers from primary MELD-based allocation and rescue allocation from 2012 to 2014 were analyzed. Primary outcome data were provided by the Eurotransplant registry. The compound endpoint "successful transplant" included: 1) 90-days patient survival without 2) a retransplant for primary graft dysfunction or 3) an indication for relisting within 90 days after transplant.
**Results:** From 2012 to 2014 $n = 325$ liver organ offers were handled by our team. The organ refusal rate (ORR) was similar for different surgeons (ORR 57–68%) A trend towards higher ORR was found for early-hour offers (12 pm – 8 am 74%). Reasons for refusal were size (22%), elevated liver enzymes (14%), organ quality (13%), recipient readiness (8%), BMI (6%) and age (5%). However, no significant differences were found between declined and accepted liver offers with respect to age (56.2 vs. 53.3 years), male gender (56 vs. 56%), BMI (27 vs. 26), cause of death, BAR-Score (12.8 vs. 9.9) and DRI (1.8 vs. 1.6).

125 of 201 (62%) liver organ offers, that were declined by our team, were transplanted elsewhere after a total of 13.2 offers per donor. Relisting or death
**Conclusion:** These findings suggest that the majority of declined organs could be successfully transplanted. A poor donor-recipient match may be a component of the high rate of declined organs. However, we cannot exclude that a proportion of wait list mortality results from declined, rather than lack of opportunity, for transplantation. Therefore, decision making whether to accept or not an offered organ has to be critically appraised in the context of severe organ shortage.

**LONG-TERM COMPLICATIONS**

## V56 PREVALENCE OF DIABETES AND PREDIABETES AMONG KIDNEY TRANSPLANT WAITING LIST CANDIDATES

*M. Guthoff[1], D. Vosseler[1], J. Langanke[1], H.-U. Häring[1], A. Königsrainer[2], S. Nadalin[2], N. Heyne[1]

[1]Abteilung für Endokrinologie und Diabetologie, Angiologie, Nephrologie und Klinische Chemie, Universitätsklinikum Tübingen, Tübingen, Germany; [2]Allgemeine, Viszeral- und Transplantationschirurgie, Tübingen, Universitätsklinikum Tübingen, Germany

**Purpose:** Diabetes mellitus (DM), the most common cause of ESRD, limits access to transplantation and impairs patient and allograft outcome. Prediabetes is an independent risk factor for progression to overt DM, as well as post-transplant DM. Albeit a modifiable risk factor, a paucity of data exists on the prevalence on kidney transplantat waiting list.
**Methods:** The active kidney transplant waiting list of a large European university hospital transplant center was metabolically phenotyped using oral glucose tolerance test. Indices for insulin sensitivity and secretion were calculated.
**Results:** Of the 138 patients investigated, 30 (22%) had known diabetes mellitus, 14 with type 1 DM and 16 with type 2 DM. 4 patients (3%) were newly diagnosed with diabetes mellitus, 39 patients (28%) were detected to have prediabetes. Overall, more than half of patients on active waitlist (53%) showed disturbances in glucose metabolism.
**Conclusion:** We demonstrate the prevalence of DM or prediabetes on kidney transplant waitlist to be as high as 53%, with more than 30 % of patients previously undiagnosed. Considering prognostic implications, strategies to reduce patient risk prior to and following transplantation are warranted. Our data provide a basis for early risk stratification and intervention to improve patient and allograft outcome.

**IMMUNOSUPPRESSION/NOVEL STUDIES**

## V59 IMMUNOGLOBULIN INDUCTION THERAPY IN RENAL TRANSPLANT RECIPIENTS – FIVE YEAR DATA OF A PROSPECTIVE RANDOMIZED PILOT STUDY

*B. Bartylak[1], A. Staak[1], F. Renner[1], C. Süsal[2], H. Dietrich[1], L. Rainer[1], W. Padberg[3], G. Opelz[2], R. Weimer[1]

[1]Department of Internal Medicine, University of Giessen, Giessen, Germany; [2]Institute of Immunology, University of Heidelberg, Heidelberg, Germany; [3]Department of Surgery, University of Giessen, Giessen, Germany

Intravenous immunoglobulin (IVIG) administration provides an established treatment modality to reverse steroid resistant rejection and to suppress alloantibody formation in sensitized recipients. To analyze graft protective effects of IVIG induction therapy, we performed a prospective randomized study in 50 renal transplant recipients who were randomly assigned to receive 7 × 10 g IVIG and 7 × 10 g iv albumin infusions, respectively.

IVIG induction therapy did not affect sCD30 and sIL1-RA levels, but regulatory autoantibody levels were increased on day 10 (IgG anti-Fab and anti-$F(ab)_2$: $P \leq 0.005$; IgA anti-Fab, anti-$F(ab)_2$ and anti-hinge: $P < 0.05$). IVIG patients showed an enhanced monocyte IL-10 production early post-transplant (day 30: $P = 0.011$, unstimulated; $P = 0.049$, LPS), followed by downregulated monocyte activation ($P = 0.024$, 4-month neopterin) and profoundly suppressed 1-year CD4 helper activity compared to non-IVIG patients ($P = 0.003$; logistic regression: $P = 0.001$). However, IVIG induction had no impact on 5-year patient and graft survival, graft function, incidence of acute rejections, chronic graft dysfunction and severe infectious diseases.

Our data show that IVIG induction is associated with potentially graft protective immunological effects (regulatory autoantibody levels, monocyte IL-10 production and activation, profoundly decreased CD4 helper activity at 1 year). However, no improved clinical outcome was found up to 5 years posttransplant in this cohort of immunologically low-risk patients.

## V60 FINAL RESULTS FROM THE LONG-TERM EXTENSION (LTE) OF THE BELATACEPT PHASE 2 STUDY IN KIDNEY TRANSPLANTATION

*G. Grannas[1], C. Larsen[2], J. Grinyo[3], F. Mühlbacher[4], G. Blancho[5], B. Charpentier[6], C. Jones-Burton[7], F. Vincenti[8]

[1]Medizinische Hochschule, Hannover, Germany; [2]Emory University, Atlanta, GA, USA; [3]Hospital Universitari de Bellvitge, Barcelona, Spain; [4]Medical University of Vienna, Vienna, Austria; [5]University Hospital Nantes, Nantes, France; [6]University Hospital of Bicêtre, Le Kremlin-Bicêtre, France; [7]Bristol-Myers Squibb, Princeton, USA; [8]University of California at San Francisco, San Francisco, USA

**Background:** At 5 years post-transplant, data from the Phase 2 IM103-100 LTE study of belatacept in kidney transplantation demonstrated a favorable safety profile and improved renal function vs. cyclosporine (CsA) (Vincenti F et al, *JASN* 2010;21(9):1587–96). The safety and efficacy of belatacept up to study closure (9–11 years follow-up) is reported herein.
**Methods:** Of 218 patients were randomized to receive a more or less intensive regimen of bela ($n = 145$) or CsA ($n = 73$), with bela patients receiving treatment at 4- or 8-week intervals (5 mg/kg after 6 months). Here we focus on the results of the 44 bela patients who remained in the LTE cohort until study end; too few CsA patients ($n = 9$) remained at the end of the study to make comparisons between groups.
**Results:** The 44 patients remaining in the bela group at study end received treatment for a mean of 9.7 years. From randomization to end of study, 25% of patients missed no infusions, and 21% missed only 1 infusion. There were no deaths or graft losses in this cohort. From randomization to study end, 84% of bela patients had serious AEs, 36% had serious infections, and 23% had malignancies. There were no cases of PTLD in this cohort. In the pooled bela cohort, mean (SD) MDRD cGFR was 70 (21) ml/min/1.73 $m^2$ at Month 3 and 72 (17) ml/min/1.73 $m^2$ at the end of the study. From randomization to study end, there was 1 acute rejection episode (Banff grade IIA), occurring in Year 9 in a patient randomized to the 8-week dosing interval group.
**Conclusions:** Data suggest that the profile of belatacept is consistent over approximately 10 years of treatment: patients maintained renal function with no new safety findings and there was high treatment compliance. However, the sample sizes are limited in this self-selecting cohort, therefore results should be interpreted with caution.

## V61 COMPARISON OF THE CALCINEURIN INHIBITORS TACROLIMUS AND CYCLOSPORINE IN COMBINATION WITH EVEROLIMUS IN HEART TRANSPLANT RECIPIENTS WHO SURVIVED 1 YEAR AND LONGER

*U. Fuchs, A. Zittermann, S. Ensminger, M. Wasgien, O. Gärtner, U. Schulz, J. Gummert

Thorax – und Kardiovaskularchirurgie, HDZ NRW, Bad Oeynhausen, Germany

The mTOR inhibitor everolimus (EVL) is used for calcineurin inhibitor-sparing immunosuppression in heart transplantation (HTx). However, comparable data regarding clinical outcomes in HTx recipients receiving EVL either with dosage reduction of cyclosporine A (CSA) or with dosage reduction of tacrolimus (TAC) is lacking. In a retrospective data analysis, we compared 5-year clinical outcomes in 154 maintenance patients receiving EVL with CSA ($n = 106$) or TAC ($n = 48$). The primary endpoint was a composite of death, graft loss and EVL discontinuation (treatment failure). Secondary endpoints were kidney function, cardiac rejection, cytomegalovirus infection and biochemical safety parameters. In the CSA and TAC group, the primary endpoint was reached by 59.8% and 53.1%, respectively ($P = 0.716$). Five-year mortality was 30.4% (CSA group) and 23.13% (TAC group), respectively ($P = 0.371$), and freedom from EVL discontinuation was 53.3% and 59.6% ($P = 0.566$) in the respective groups. Covariate-adjusted relative risk of treatment failure was in the CSA group = 1.28 (95% CI:0.70–2.34; $P = 0.43$) compared with the TAC group. The course of covariate-adjusted estimated glomerular filtration rate and cytomegalovirus infection was similar in the two groups ($P = 0.502$), whereas freedom from rejection was lower in the CSA group compared with the TAC group ($P = 0.023$). Lipid status and blood cell counts were comparable between groups. In conclusion, data indicate that EVL plus reduced TAC is not superior to EVL plus reduced CSA regarding treatment failure and kidney function. Both study groups showed high EVL discontinuation rates.

## V62 SUPERIOR RENAL FUNCTION IN AN EVEROLIMUS-BASED CALCINEURIN INHIBITOR FREE REGIMEN COMPARED TO STANDARD CYCLOSPORINE/MYCOPHENOLATE AND LOW CYCLOSPORINE/EVEROLIMUS: FOLLOW-UP OF THE HERAKLES STUDY AT MONTH 36

*M. Guba[1], K. Budde[1], C. Sommerer[1], H.-H. Neumayer[1], F. Lehner[1], P. Reinke[1], I.A. Hauser[1], P. Weithofer[1], T. Rath[1], D. Bäumer[2], M. Porstner[2], J. Jacobi[1], M. Zeier[1], O. Witzke[1], W. Arns[1]

[1]HERAKLES Study Group, Germany; [2]Novartis Pharma, Germany

**Purpose:** To follow up (FU) on renal function (RF) at month (Mo) 36 after kidney transplantation (Tx) in patients (pts) on immunosuppressive regimen with different calcineurin inhibitor (CNI) exposures.
**Methods:** Of 802 pts were included in a 1 year, prospective, open-label, randomized (RDZ), multi-center study. After induction with basiliximab all pts received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3Mo post Tx 499 pts were RDZ 1:1:1 to either a) continue standard (STD) CsA (100–180 ng/ml) with EC-MPS ($n = 166$), b) convert to a CNI-free regimen with everolimus (EVR;5–10 ng/ml) +EC-MPS ($n = 171$) or c) convert to CNI-low regimen CsA (50–75 ng/ml) with EVR (3–8 ng/ml) ($n = 162$). Mo36 FU visit was performed by 123(89%) STD, 130(95%) CNI-free and 123(94%) CNI-low pts.
**Results:** Median trough levels: CsA 98 ng/ml in STD, 72 ng/ml in CNI-low pts; EVR 6.0 ng/ml in CNI-free, 5.4 ng/ml in CNI-low pts. RF (Nankivell) was similar at RDZ 3Mo post Tx and had significantly improved at Mo12 by +5.6 ml/min (95%CI:[+2.9;+8.3]; $P < 0.001$) and remained significantly improved by +7.0 ml/min in favor of CNI-free regimen at Mo36($P = 0.009$). 58% of CNI-free, 36% of CNI-low and 46% of STD pts had an improvement in RF at Mo36 ($P = 0.04$ CNI-free vs. STD). All 3 groups had similar rejection rate since RDZ (13%STD, 15%CNI-free, 14%CNI-low) and overall comparable safety profile.
**Conclusion:** CNI-free as well as reduced CNI in combination with EVR are both efficacious and safe regimen. The CsA trough levels in CNI-low group didn't fully meet reduction, that might have hampered to translate into better RF compared to STD. However, CNI-free regimen lead to better RF maintained for 3 years post Tx. The results of this large trial confirm previous reports of improved RF after CsA withdrawal with EVR in combination with EC-MPS.

## V63 EVEROLIMUS, MTORC1 INHIBITION, AND IMPACT ON HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION – 12, 24, AND 36 MONTHS DATA FROM 719 LTX RECIPIENTS

*G. Junge, L. Fischer, P. Schemmer, A. Speziale, H. Schwende, B. Nashan, P. Neuhaus, H.J. Schlitt
H2304 Study Group, Basel, Switzerland

**Background:** For patients with localized hepatocellular carcinoma (HCC) who don't qualify for surgical resection, LTx is an appropriate strategy for candidates with a single lesion ≤5 cm, up to three separate nodules, none larger than 3 cm (Milan criteria), no evidence of gross vascular invasion, and no regional nodal or extrahepatic distant metastases. Because immunosuppression to reduce the incidence of acute rejection is associated with higher tumor recurrence, efforts have been underway to reduce doses and to evaluate new treatment options to reduce this risk.
**Methods:** Data were retrieved from study H2304 (NCT00622869) and its extension, a 3-year RCT in 719 de novo LTx recipients comparing everolimus (EVR, C0 3–8 ng/ml) plus reduced tacrolimus (rTAC, C0 3–5 ng/ml), or EVR (C0 6–10 ng/ml) with TAC Withdrawal (TAC-WD) at M4 to standard TAC (TAC-C, C0 6–10 ng/ml). Here, we present HCC recurrence, patient outcome and impact of everolimus treatment and exposure in 203 HCC patients at 12, 24, and 36 months after LTx.
**Results:** Baseline demographics and HCC characteristics were comparable: $n = 67$, 76, 60 patients with HCC; mean age 58.4, 58.6, 58.4 years; male gender 53 (79.1%), 56 (73.7%), 52 (86.7%); average weight 75.1, 74.3, 74.1 kg; prior tumor treatment 33/67, 41/76, 27/60; within Milan criteria 60 (89.6%), 65 (85.5%), 51 (85.9%); average number of lesions 1.6, 1.6, 1.6; largest diameter (mean) 2.7, 4.0, 5.4 cm; total tumor diameter (mean) 4.1, 4.4, 4.2 cm; AFP positive 46 (68.7%), 52 (68.4%), 47 (78.3%); mean AFP level 99.7, 53.9, 34.0 ng/ml in the EVR/rTAC, TAC-WD, and TAC-C arm, respectively.

HCC recurrence was observed in 2, 12, and 14 patients at M12, 24 and 36. HCC recurrence was lower in patients treated with everolimus. Detailed data by treatment, exposure and risk factor analyses will be presented.
**Conclusion:** Everolimus, an inhibitor of the mammalian target of rapamycin (mTOR inhibitor), may offer an alternative immunosuppressive agent with intriguing prospects in patients transplanted for HCC.

## V64 THE INFLUENCE OF IMMUNOSUPPRESSIVE DRUGS ON THE EPITHELIAL MICROENVIRONMENT IN SOLID ORGAN TRANSPLANTATION

*A. Akhdar, B. Mueller, C. Neudoerfl, M. Stevanovic-Meyer, J. Keil, C. Falk
Institute of Transplant Immunology, Hannover Medical School, Hannover, Germany

**Background:** In the context of kidney and liver transplantation, NK cells play an important role by recognizing the allogeneic organ. The specific interaction with the allogeneic tissue can activate NK cell function and mediate allograft rejection. Here, we investigated the effect of immunosuppressive drugs on proliferation and chemokine production of epithelial cells.
**Methods:** Renal and liver cells were incubated with Cyclosporin A, Tacrolimus, Rapamycin, Everolimus, Mycophenolate mofetil (MMF) and Mycophenolic Acid (MPA) for 48 h. Surface expression of T/NK cell ligands by FACS and production of chemokines and phosphorylation of Akt/mTOR pathway components were analyzed by the Bioplex technique.
**Results:** CNI and mTORi down modulate CD166, CD155 and HLA class I surface expression on HEK293, HepG2 and Huh7 cells and CD166 expression on RCC26. mTORi inhibited significantly kinases of the PI3K/Akt pathway in renal cell lines, while CNI had no effect. In liver cell lines Rapa and Ever inhibited the PI3K/Akt pathway. In contrast CsA and MMF induced activation of the mTOR pathway in Huh7. Chemokine secretion was also influenced by immunosuppressive drugs. In HEK293 cells, CXCL12 was suppressed by Rapa and CsA. MIF was significantly suppressed by Rapa, Ever, CsA, Tac, MMF and MPA. In RCC26 cells, CXCL8 was suppressed by CsA, Tac and MMF. In Hep3B cells, CXCL8 and VEGF were suppressed by Rapa, CsA, MMF and MPA. In contrast, in HepG2 and Huh7 cells, Follistatin and Leptin were induced by Ever and Tac.
**Conclusion:** Our results demonstrate that CNI as well as mTORi are able to modulate the microenvironment and surface expression of T and NK cell ligands on kidney and liver cells. However, mTORi, but not CNI inhibit the PI3K/Akt pathway in renal cell lines. In liver cell lines, both mTORi and CNI suppressed the mTOR pathway. Chemokine secretion was impaired upon immunosuppressive treatment, which may be important for the prevention from graft rejection. Taken together, it may be important to suppress the chemokine secretion by epithelial cells, so that the immune system would not be able to respond against the transplanted organ and starts a graft rejection.

**LIVING DONATION**

## V65 OUTCOME ON RENAL FUNCTION, EFFICACY AND SAFETY IN LIVING-DONOR KIDNEY TRANSPLANT RECIPIENTS AFTER CONVERSION FROM A CALCINEURIN INHIBITOR TO AN EVEROLIMUS BASED REGIMEN: A POST HOC SUBGROUP ANALYSIS OF ZEUS

*F. Lehner[1], K. Budde[1], R.P. Wüthrich[1], O. Witzke[1], M. Zeier[1], I.A. Hauser[1], H.H. Wolters[1], B. Suwelack[1], K. Heller[1], P. Reinke[1], W. Arns[1], R. Stahl[1], A. Mühlfeld[1], U. Eisenberger[1], D. Bäumer[2], M. Porstner[2], C. Sommerer[1]
[1]ZEUS Study Group, Germany; [2]Novartis Pharma, Germany

**Aim:** To study renal function and patient outcome in living donation subgroup of kidney de novo transplant recipients after conversion to an everolimus (EVR) based regimen and withdrawal of calcineurin inhibitor (CNI) therapy. Methods: Post hoc subgroup analysis from the prospective, open-label, controlled, multicenter study ZEUS. 300 renal transplant (Tx) patients (pts) were randomized (rdz) at month (Mo) 4.5 post Tx to either EVR plus enteric coated-mycophenolate sodium (EC-MPS) or cyclosporine (CsA) plus EC-MPS regimen, among them 80 living donor recipients (EVR $n = 42$; CsA $n = 38$).
**Results:** In liv.donor recipients subpopulation, adjusted estimated GFR (Nankivell) at Mo12 (primary endpoint) was 74.3 (95%CI [70.7, 77.9]) ml/min/1.73 $m^2$ in EVR vs. 63.8 (95%CI [60.0, 67.7]) ml/min/1.73 $m^2$) in CsA group, i.e. 10.5 ml/min/1.73 $m^2$ difference in favor of EVR ($P < 0.001$). From rdz to Mo12, mean adj.estimated GFR was +9.8 (95%CI [6.2, 13.4]) ml/min/1.73 $m^2$ in the EVR subgroup, versus −0.7 (95%CI [−4.6, 3.1]) ml/min/1.73 $m^2$) ($P < 0.001$) within CsA group since rdz. Of 6 BPAR episodes in the EVR group, 5 were Banff I graded. Overall safety profile was similar between treatment groups. Discontinuation due to adverse events occurred in 3 EVR-treated (7.1%) and 5 CsA-treated pts (13.2%) between rdz and Mo12.
**Conclusion:** EVR-based regimen with early elimination of CNI therapy in living donor kidney transplant recipients is associated with a significant renal benefit at 12Mo post Tx without compromising safety and efficacy.

## V68 A BODY MASS INDEX (BMI) GREATER THAN 30 IS NOT A CONTRAINDICATION FOR LIVE DONOR LIVER TRANSPLANTATION (LDLT)

*J.M. Knaak[1], V.N. Spetzler[2], N. Selzner[2], D.R. Grant[2], G. Levy[2], M. Selzner[2]
[1]Allgemein- und Viszeralchirurgie, Frankfurt am Main, Universitätsklinikum Frankfurt am Main, Germany; [2]MultiOrganTransplant, Toronto General Hospital, Toronto, ON, Canada

Obesity is dramatically increasing in Western countries, and accordingly, many potential donors interested in living liver donation are obese. We investigated if adult-to-adult living donor liver transplantation using living donors with a BMI>30 vs. <30 is safe for the donor and provides comparable recipient outcomes.
**Methods:** We investigated 320 adult-to-adult living liver transplantation performed in a single institution between December 2000 and December 2013. We compared donor and recipient outcome of 78 donors wit a BMI >30, with 242 donors with a BMI <30. Steatosis was <10% in all donor livers, as confirmed by imaging and biopsy.
**Results:** BMI of the obese (35 + 6) vs. lean donors (24 + 3) was significantly increased ($P < 0.01$). No difference existed between obese and lean donors regarding donor age, gender, and residual liver volume. Donor hepatectomy in lean vs. obese donors was associated with similar blood loss (898 + 346 cc vs. 1090 + 452 cc, $P = 02$), transfusion requirement (2% vs. 0%, p- = 0.6), and duration of surgery (7.3 + 1.3 h vs. 7.6 + 1.3 h, $P = 0.2$). No difference was observed between both donor groups regarding peak AST, ALT, INR or bilirubin after hepatectomy. 23%of lean vs. 27% of obese donors experienced a complication after surgery. Dindo-Clavien Grad 3b complications occurred in 3.8% of lean vs. 2.3% of obese donors ($P = 0.7$), no grad 4 or 5 complication was observed. Median hospital stay was 7 days in both donor groups. Recipient outcome was comparable with no difference regarding peak AST, ALT,INR and bilirubin levels within the first week after transplantation. Recipients of the lean vs. obese donor group had similar 5-year graft (71% vs. 76%, $P = 0.64$) and patient (76% vs. 79%, $P = 0.64$) survival.
**Conclusion:** Living liver donation of obese donors is safe in the absence of steatosis and provides similar donor and recipient outcomes in a carefully selected donor population.

**MISCELLANEOUS**

## V69 ORGAN DONATION AND TRANSPLANTATION- ATTIDUDES OF MEDICAL PROFESSIONALS INVOLVED

*T. Breidenbach[1], T. Bein[2], J. Briegel[3], K.-U. Eckardt[4], G. Gerresheim[5], C. Lang[4], C. Nieß[6], F. Zeman[2,6], D. Grammenos[1]
[1]Deutsche Stiftung Organtransplantation, München, Germany; [2]Universitätsklinikum Regensburg, Regensburg, Germany; [3]LMU, München, Germany; [4]Universitätsklinikum Erlangen, Erlangen, Germany; [5]Klinikum Neumarkt, Neumarkt, Germany; [6]Deutsche Stiftung Organtransplantation, Frankfurt, Germany

**Objective:** Attitudes of medical personnel are crucial in the process of organ donation. We conducted a survey to find out the attitudes of hospital staff towards organ donation and transplantation.
**Methods:** The medical staff in 50 Bavarian hospitals were asked to respond anonymously to a questionnaire.
**Results:** Of 2983 questionnaires could be evaluated. The majority of all respondents had a positive attitude towards organ donation; 71% were willing to donate their organs after brain death and 57% were willing to accept a transplant in case of organ failure. Rates of positive attitude were lower among nurses than among physicians. The majority of nurses and a large proportion of physicians considered themselves as not well informed.
**Conclusion:** Although the attitude of medical personnel to organ donation is more positive than it has been reported in the general population, the responses reflect concerns in a substantial proportion of health care professionals, which may represent important hurdles to organ donation, often caused by a lack of information. Therefore, it is necessary to improve the knowledge of the medical staff.

## V70 TRANSPLANT SURGERY IN GERMANY: RESULTS OF A NATION-WIDE SURVEY

*M. Thomas[1], S. Nadalin[2], P. Schemmer[3], A. Pascher[4], G. Kaiser[5], F. Braun[6], B. Nashan[7], T. Becker[6], M. Guba[1]
[1]Klinik für Allgemeine-, Viszeral-, Transplantations-, Gefäß- und Thoraxchirurgie, Klinikum der Universität München, München, Germany; [2]Universitätsklinik für Allgemeine, Viszeral- und Transplantationschirurgie, Universitätsklinikum Tübingen, Tübingen, Germany; [3]Klinik für Allgemein-, Viszeral- und Transplanationschirurgie, Universitätsklinikum Heidelberg, Heidelberg, Germany; [4]Klinik für Allgemein-, Visceral- und Transplantationschirurgie, Charité – Universitätsmedizin Berlin- Campus Virchow-Klinikum, Berlin, Germany; [5]Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Universitätsklinikum Essen, Essen, Germany; [6]Klinik für Allgemeine Chirurgie, Viszeral-, Thorax-, Transplantations- und Kinderchirurgie, Universitätsklinikum Schleswig-Holstein, Kiel, Germany; [7]Klinik und Poliklinik für Hepatobiliäre Chirurgie und Transplantationschirurgie, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany

We have conducted a nation-wide survey on demographics, training, position, individual case loads, center volumes, program structure, professional practice, grade of specialization, workload, working-hours, salary and career expectations of transplant surgeons in Germany.

Transplant surgeons of 32 German transplant centers were asked to participate on this survey. There were 85 respondents who were 43 ± 8 years of age and predominantly male (85%). Most transplant surgeons were fully trained general and visceral surgeons. Only, few surgeons have formal specialty training in transplantation. Clinical transplant practice included, kidney, liver and pancreas transplantation, living-donor procedures and pediatric transplantation. Overall, the grade of specialization was low. Transplantation was rated to be only 10–25% of the operative clinical practice and most surgeons considered themselves as hepatobilary surgeons and only second-line as transplant surgeons. The individual caseload per active surgeon was low (e.g. 16 deceased liver transplant procedures/a, 16 kidney transplant procedures/a and 3 pancreas transplant procedures/a). The majority of transplant surgeons reported working hours of 66 h/week and above, at least 7 days of transplant on-calls and a median of 8 (1–52) operative transplant cases a year. The majority of surgeons reported an annual salary between 80 and 125.000€. Only 60% of the transplant surgeons would recommend following a transplant surgeon career. This is the first study assessing the professional life of transplant surgeons in Germany. The results of this survey should be taken into account by the setup of current and new transplant positions in Germany.

## V71 ABDOMINAL WALL TRANSPLANTATION: A SENTINEL MARKER FOR REJECTION?

*U. Gerlach[1,2], H. Giele[3], G. Vrakas[2], S. Reddy[2], A. Pascher[1], P. Friend[2], J. Pratschke[1], A. Vaidya[2]
[1]Abt.für Allgemein-, Viszeral- und Transplantatiosnchirurgie, Charité Berlin, Berlin, Germany; [2]Department of Transplant Surgery, Oxford University Hospitals and University of Oxford, Oxford, UK; [3]Department of Plastic and Reconstructive Surgery, Oxford University Hospitals and University of Oxford, Oxford, UK

Abdominal wall transplantation (AWT) has revolutionized difficult abdominal closure after intestinal transplantation (ITX) in eligible patients. The pioneering immunological benefit is however to precociously detect and treat rejection (skin rash on AWT), before it manifests in the intestine thus avoiding severe bowel dysfunction; and the ability to distinguish it from infection (no skin rash before bowel dysfunction).

Between 2012 and 2014, twelve patients (mean age 42 ± 13 years) received AWT to complement ITX from the same donor at the Oxford Transplant Centre. Two doses of Alemtuzumab were used for induction therapy (30 mg, 6 and 24 after reperfusion) Tacrolimus (trough levels 8–12 ng/ml) was used for maintenance immunosuppression.

Three recipients had biopsy proven rejection of the skin on their AWT. These patients did not demonstrate concurrent intestinal graft rejection. In contrast, in one patient with bowel dysfunction (fever,diarrhoea), the skin of the AWT remained normal. Intestinal histology was reported as CMV disease.

The skin component of the AWT may serve as a sentinel marker for immunological activity in the host. This is a vital tool for timely prevention of intestinal graft rejection and more importantly the avoidance of overimmunosuppression in cases where bowel dysfunction manifests without the skin component being affected.