SHORT PRESENTATIONS ON POSTERS

PV001 POSTOPERATIVE RISK FACTORS OF ORGAN TRANSPLANT RECIPIENTS FOLLOWING DERMATOSURGICAL PROCEDURES

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Introduction and Background: Organ transplant recipients (OTRs) have a greater risk of developing malignant skin tumors than the general population. In addition these skin tumors behave more aggressively and metastasize more frequently. The aim of our study was to investigate whether OTRs have an increased incidence and a different postoperative risk profile than the general dermatosurgical patient population.
Methods: Our study comprised of 2.325 patients (222 OTRs) who presented to the dermatosurgical department of the University Clinic Essen between 1 January 2008 until 31 December 2011. The patients underwent dermatosurgery for one of the following malignant skin tumor; basal cell carcinoma, squamous cell carcinoma, Bowen's disease, malignant melanoma, Kaposi's sarcoma, Merkel-cell carcinoma and malignant adnexal tumors. Our study focused on several postoperative risk factors; wound infection, development of seroma, sepsis, rebleeding, suture dehiscence, flap necrosis, nerve damage, wound healing disorder and lymph edema.
Results and Conclusions: The sum of all postoperative complications did not differ between all OTRs and the control group ($P > 0.05$). However the risk of different postoperative complications varied between OTRs and the control group. OTRs developed postoperative bleeds more frequently ($P = 0.0064$), which can be caused by the immunosuppressive medication and the higher incidence of Diabetes mellitus and anemia. In contrast to current research the OTRs in our study developed wound infections less frequently ($P = 0.0294$). Possible causal factors are; an increased number of perioperative and long-term antibiotic treatments, a greater amount of wound closure via secondary wound healing as well as closer dermatological monitoring.

PV002 TACROLIMUS CONCENTRATION/ DOSE RATIO INFLUENCES BKV INFECTION AFTER KIDNEY TRANSPLANTATION

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Introduction and Background: BK virus (BKV) infection is a serious complication following renal transplantation (RTx). The minimization of risk factors that predict BKV infection might help to prevent BKV associated nephropathy (BKN). Given that immunosuppression promotes BKV infection, we hypothesized an association between tacrolimus (Tac) metabolism rate and BKV infection.
Methods: RTx patients with BK viremia (BKV group) were compared with BKV negative recipients that presented at our transplant centre. The Tac metabolism rate expressed as the blood concentration normalized by the daily dose (C/D ratio) was used to assess the Tac metabolism rate. Tac trough blood levels, daily Tac doses and prednisolone doses were analyzed at 1, 3 and 6 months after RTx.
Results and Conclusions: 96 BKV positive patients were compared with 96 BKV negative controls. BKV was detected after a median time of 4 (0–64) months after RTx. The BKV group was older (54.4 ± 13.2 vs. 50.3 ± 14.7; $P = 0.045$) and included more CMV high risk patients (D+/R−) (29.2% vs. 9.4%; $P = 0.0007$). BKV positivity was associated with a lower Tac C/D ratio (fast metabolizers) at 1, 3 and 6 months after RTx. Mean Tac trough levels were lower 1 and 6 months after RTx in the BKV group ($P = 0.0024$; $P = 0.0013$, respectively). Mean daily Tac doses did not differ noticeably between the groups. As a known inductor of Tac metabolism, the prednisolone dose was noticeably higher in patients with BKV infection 3 months after RTx ($P = 0.0098$). Using logistic regression analysis, age, CMV high risk status and fast Tac metabolism were associated with BKV infection. 9.4% of all BKV positive patients revealed histologically proven BKN.

We conclude from our data that recipient age, CMV high risk status and faster Tac metabolism are associated with BKV infection after RTx. The Tac C/D ratio should be taken into account in BKV risk stratification.

PV003 TUMOR RISK IN PATIENTS AFTER LONG-TERM KIDNEY TRANSPLANTATION

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Introduction and Background: Since 40 years kidney transplantation has been established in Europe therefore the number of long-term transplanted patients as well as the risk for developing post-transplant tumors has raised. In our kidney transplant population genesis, incidence and therapy of tumors were analyzed to identify risk factors with special regard to the long-term immunosuppression therapy.
Methods: Between 1984 and 2016 the data of 1850 kidney transplanted patients were examined by multivariate analysis to find out significant factors for cancer development in long-term transplanted patients.
Results and Conclusions: 12.5% of all patients developed cancer disease, most of them 72% skin cancer, but in nearly 20% solid cancer was found. The average time for the tumorigenic process was 11.3 years (2-26 years). Strong immunosuppression therapy in patients with high immunological risk (retransplantation, % of PRA, number and grade of rejection) seem to be a decisive factor for cancer development. Discussion: Tumor risk factors, as well as established screening modalities for the single types of tumors and recommendations of therapy strategies were presented and discussed.

PV004 KIDNEY TRANSPLANT RECIPIENTS AFTER PREVIOUS NONRENAL TRANSPLANTATION SHOW LOW ALLOREACTIVITY BUT AN INCREASED RISK OF INFECTIOUS COMPLICATIONS

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Introduction and Background: The number of kidney transplant recipients (KTRs) after nonrenal solid organ transplantation (SOT) is increasing to 3–5% of all kidney transplantations. Knowledge on patient and allograft outcomes, however, remains scarce.
Methods: We studied 40 KTRs after nonrenal SOT. 720 primary KTRs and 119 repeat KTRs were used for comparison. Samples were collected pretransplantation, at +1, +2, +3 months posttransplantation. Alloreactive and CMV-specific T-cells were measured using an interferon-γ Elispot assay.
Results and Conclusions: KTRs after nonrenal SOT show comparable patient survival, death-censored allograft survival and allograft function compared with primary KTRs, but superior death-censored allograft survival and function compared to repeat KTRs ($P < 0.05$). Interestingly, KTRs after nonrenal SOT show less preformed panel-reactive antibodies, alloreactive T-cells, and acute rejections compared to repeat KTRs ($P < 0.05$). KTRs after nonrenal SOT, however, show higher incidences of EBV-viremia and PTLD, septic complications, and death from sepsis ($P < 0.05$). A tendency of impaired CMV-specific cellular immunity was associated with more CMV-replication compared to repeat KTRs.

Our results suggest comparable patient and allograft outcomes in KTRs after nonrenal SOT and primary KTRs. The observed low alloreactivity may contribute to superior allograft outcomes compared to repeat KTRs. Caution should be taken in KTRs after nonrenal SOT regarding over-immunosuppression with viral replication and sepsis.

Our results suggest patient and allograft outcomes in KTRs after SOT other than kidney comparable to KTRs of a first kidney allograft. The observed low alloreactivity may be attributed to the effects of maintenance immunosuppression. Caution should be taken in KTRs after SOT other than kidney regarding overimmunosuppression with development of EBV viremia and septic complications.

PV005 VALIDATION OF A NOVEL CYTOMEGALOVIRUS-SPECIFIC ELISPOT ASSAY TO MONITOR THE FUNCTIONALITY OF CELL-MEDIATED IMMUNITY IN HEMODIALYSIS PATIENTS

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Introduction and Background: Impairment of cytomegalovirus (CMV)-specific cell-mediated immunity (CMI) by immunosuppressive therapy is a major cause for CMV reactivation and associated complications in solid organ transplantation. Assessing the function of CMV-specific CMI may help to individually adjust immunosuppressive as well as antiviral therapy. The novel T-Track® CMV assay allows the simultaneous detection of CMV-reactive T-helper and cytotoxic T cells using T-activated® pp65 and IE-1 proteins for *in vitro* restimulation of PBMC and an IFN-γ ELISpot for quantification of reactive cells. The aim of this study was to evaluate the suitability of T-Track® CMV for monitoring CMV-specific CMI in a clinically relevant pre-transplant patient population.
Methods: Sensitivity and specificity of T-Track® CMV were examined in a cohort of 124 hemodialysis patients of whom 67 (54%) revealed a CMV-positive serostatus. The results of the T-Track® CMV assay were compared to that of QuantiFERON®-CMV and of a cocktail of 6 preselected CMV tetramers as reference tests.
Results and Conclusions: Positive T-Track® CMV results were obtained in 60/67 (sensitivity 89.6%) of CMV-seropositive hemodialysis patients, and were dominated by pp65-reactive cells (58/67 or 86.6%). In comparison, QuantiFERON®-CMV and CMV tetramer cocktail revealed sensitivities of 72.6% (45/62) and 76.9% (40/52) respectively. 12/57 CMV-seronegative patients demonstrated positive T-Track® CMV results, mostly in response to T-activated® IE-1 stimulation, confirming data showing IE-1-specific T cell responses in seronegative individuals. T-Track® CMV is therefore a highly standardized and sensitive test that can be used in a broad population of patients, independently of their HLA-type. T-Track® CMV is currently evaluated in clinical multi-center studies for renal and allogeneic stem cell transplantation patients, to further assess its use for the risk assessment and prediction of CMV-related clinical complications.

PV007 CLINICAL VALIDATION OF T-TRACK® CMV TO ASSESS THE FUNCTIONALITY OF CMV-SPECIFIC CELL-MEDIATED IMMUNITY IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Background: Impairment of cytomegalovirus (CMV)-specific cell-mediated immunity (CMV-CMI) by immunosuppressive therapy is a major cause for CMV reactivation and associated complications in solid organ transplantation (Tx). Assessing the functional impairment of CMV-CMI may help to individually adjust immunosuppressive as well as antiviral therapy. The aim of this study was to evaluate the suitability of T-Track® CMV, a novel immune-monitoring assay to survey CMV-CMI in kidney Tx patients.
Methods: A prospective, longitudinal, observational, multicenter study was conducted in a cohort of 96 intermediate risk (D-/R+, D+R+) renal transplant recipients over a 6-month period post-Tx. Patients received standard immunosuppressive therapy and underwent antiviral (AV) treatment following institutional guidelines. T-Track® CMV was used to quantify CMV-reactive Th and CTL cells in response to T-activated® pp65 and IE-1 proteins using an IFN-γ ELISpot assay. CMV viral load was determined by quantitative PCR or pp65 antigenemia. CMV-related complications, opportunistic infections, and graft function were monitored.
Results and Conclusions: T-Track® CMV results were positive in 94.6% of the patients pre-Tx and in 88.1-91.4% of the patients post-Tx. T-Track® CMV was also able to measure a transient decrease in CMV-CMI following immunosuppressive treatment. Since this study was non-interventional, it is unclear whether control of CMV replication in patients who received AV treatment was the effect of CMV-CMI or of AV. However, all patients with self-limiting CMV replication (in the absence of AV treatment) showed elevated pp65-CMI (80-982 SFC/2.10^5 lymphocytes; median 384; $n = 12$) prior to CMV reactivation, suggesting that pp65-CMI might represent a potential protective marker. Altogether, this study confirmed T-Track® CMV as a suitable immune-monitoring tool following kidney Tx, with a potential use for the risk assessment of CMV-related clinical complications.

PV008 DACLATASVIR PLUS SOFOSBUVIR FOR CHRONIC HCV-INFECTED KIDNEY TRANSPLANT RECIPIENTS – A PILOT STUDY OF EFFICACY AND SAFETY

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Introduction and Background: The novel direct-acting agents (DAAs) represent a highly efficient treatment option for patients with chronic hepatitis C virus (HCV) infection. To date, there is a lack of data regarding the use of DAAs in kidney transplant recipients (KTR).
Methods: This prospective single center study evaluated a combined therapy with Daclatasvir (DAC) 60 mg and Sofosbuvir (SOF) 400 mg given over 12 weeks in $n = 11$ adult chronic HCV infected KTR. Ultrasound, MRI and liver biopsy were performed prior to treatment. Only KTR with eGFR >30 ml/min were included. Primary endpoint was defined as sustained virological response 12 weeks after the end of therapy (SVR12). Here we report the data of the interims analysis of the first 11 KTR.
Results and Conclusions: Prevalence of chronic HCV infection within the group of KTR with functioning graft was 32/1365 (2.3%) at screening. Distribution rate of genotypes revealed $n = 2$ with genotype 1a and $n = 30$ with genotype 1b. 4/11 KTR who started treatment, had a history of failed treatment with IFN therapy. Liver biopsy at screening showed a medium fibrosis score of 1.73 (according to Desment). Treatment with DAC + SOF was initiated at a median of 126.7 ± 2.4 months after kidney transplantation. At the time of this analysis, HCV RNA was not detectable in 100% ($n = 11$) of patients on DAC + SOF treatment. All patients showed a rapid virological response, defined by already undetectable viremia 4 weeks after start of therapy. To date, 4/11 KTR have achieved SVR 4 weeks after completion of therapy. Calcineurin inhibitor dose adjustment during treatment was required in 2/11 patients. The DAC + SOF therapy was well tolerated with no therapy-associated major adverse events. So far no major treatment-related side effects and no drug discontinuation were detected. Here we report the first controlled prospective study results, using DCV + SOF treatment in chronic HCV infected KTR. First safety and efficacy data in this population are shown. Additional data will be available at the date of presentation

PV009 SUCCESSFUL THERAPY OF CHRONIC HEPATITIS C VIRUS INFECTION WITH SOFOSBUVIR AND LEDIPASVIR IN RENAL TRANSPLANT RECIPIENTS

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Introduction and Background: Treatment of chronic hepatitis C virus (HCV) infection after renal allograft transplantation has been an obstacle because of contraindications associated with interferon (IFN)-based therapies. Direct-acting antiviral agents are highly efficient treatment options that do not require IFN and may not require ribavirin. Therefore we assessed efficacy and safety of sofosbuvir and ledipasvir in chronic HCV- infected renal transplant patients.
Methods: Fifteen renal allograft recipients with therapy-naïve HCV genotype (GT) 1a, 1b, or 4 were treated with the combination of sofosbuvir and ledipasvir without ribavirin for 8 or 12 weeks. Clinical data were retrospectively analyzed for viral kinetics and for renal and liver function parameters. Patients were closely monitored for trough levels of immunosuppressive agents, laboratory values, and potential adverse effects.

Results and Conclusions: Ten patients (66%) exhibited a rapid virologic response within 4 weeks (HCV GT1a, $n = 4$; HCV GT1b, $n = 6$). The other five patients exhibited a virologic response within 8 (HCV GT 1b, $n = 4$) or 12 weeks (HCV GT4, $n = 1$). 100% of patients exhibited sustained virologic response at week 12 after end of treatment. Clinical measures of liver function improved substantially for all patients. Adverse events were scarce; renal transplant function and proteinuria remained stable. Importantly, dose adjustments for tacrolimus were necessary for maintaining sufficient trough levels.
Conclusions: The described regimen appears to be safe and effective for patients after renal transplant and is a promising treatment regimen for eradicating HCV in this patient population.
* HG and UE contributed equally to this work.

PV010 A CLOSING CHAPTER – THERAPY OF HCV GENOTYPE III RECURRENCE IN LIVER TRANSPLANTS

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Introduction and Background: Historically, HCV-genotype (GT) 3 was not as hard to treat as genotype-1 HCV-infection using interferon-based therapy. Nowadays, GT-3-HCV-infection can easily be assessed using interferon-free regimes such as the combination of sofosbuvir (SOF) and daclatasvir (DCV) as a highly successful and reliable therapeutic option.

We report a successful antiviral treatment of our last 10 GT-3 patients suffering from HCV-recurrence after liver transplantation with SOF/DCV.
Methods: This report presents a descriptive analysis of 10 patients who were transplanted due to a GT-3 cirrhosis in our center. Only two of them were naïve for any antiviral therapy. All of them received antiviral treatment with SOF/DCV for 12 weeks after liver transplantation; in one case ribavirin was additionally applied. The endpoint was HCV-RNA free survival after 12 weeks of therapy. Secondary endpoints were preservation of renal and liver function and incidence of adverse events.
Results and Conclusions: All patients were free of HCV-RNA at the latest from 8 weeks of therapy. Elevated transaminases and gamma-glutamyl transferase at the beginning of therapy normalized during the therapy. Bilirubin and alkaline phosphatase were stable at all dates. There were no severe side effects especially on renal function or blood count. Sustained virological response rates at week 12 were achieved in all 10 patients.

HCV could be eliminated in all patients after liver transplantation by antiviral treatment of SOF/DCV over 12 weeks. SOF/DCV is a safe and reliable antiviral therapy of recurrent GT-3 HCV-infection that allowed us to close the chapter of HCV-recurrence after liver transplantation in our outpatient clinic.

PV011 VON WILLEBRAND FACTOR PREDICTS RETRANSPLANTATION-FREE SURVIVAL AFTER FIRST LIVER TRANSPLANTATION

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Introduction and Background: Liver transplantation (LT) is a successful treatment option for end-stage liver. After LT, liver-related, infectious and cardiovascular complications contribute to reduced graft and patient survival. These conditions are associated with an increase in von Willebrand factor antigen (VWF-Ag), which was previously also correlated with survival in cirrhotic patients. We evaluated VWF-Ag as predictive marker after LT.
Methods: We conducted a prospective study in patients after first LT treated at the University Hospital Heidelberg. Patients that were seen for follow-up after LT in the outpatient clinic of our department between November 2012 and August 2013 were screened. To be included, patients had to be at least 18 years of age at time of inclusion, and only patients after first LT were eligible. We measured VWF-Ag in these patients and followed them prospectively with regard to the primary endpoint, namely retransplantation-free survival.
Results and Conclusions: Six of the 80 patients died or received re-LT during follow-up. Median VWF-Ag was 510.6% in these patients and significantly higher ($P = 0.001$) than in the patients alive at the end of follow-up (median: 186.8%). ROC analysis (AUC: 0.914) revealed an optimal cut-off of 286.8% for prediction of the primary end-point (sensitivity: 100%, specificity: 81.1%). Survival was longer in patients with a VWF-Ag below this cut-off compared to those with a higher VWF-Ag ($P < 0.001$ according to log-rank test). VWF-Ag was associated with retransplantation-free survival in multivariate analysis as was alkaline phosphatase (ALP), but not MELD score, donor age, or cold ischemia time. A score combining VWF-Ag and ALP showed impressive capability in ROC analysis (AUC: 0.958) to distinguish between patients with regard to the primary endpoint.

VWF-Ag is a non-invasive marker to predict outcome in patients after LT. Its diagnostic performance increased when combined with ALP in a newly developed score.

PV012 *A 3-YEAR POST-HOC* ANALYSIS OF THE RANDOMIZED H2304 EXTENSION STUDY EVALUATION OF THE MAJOR ADVERSE CARDIAC EVENTS RISK WITH EVEROLIMUS-BASED CALCINEURIN INHIBITOR REDUCTION OR WITHDRAWAL REGIMEN IN LIVER TRANSPLANT RECIPIENTS

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Introduction and Background: Cardiovascular disease (CVD) is one of the leading causes of death in liver transplant recipients (LTxRs). Impaired glomerular filtration rate (GFR) is a risk factor for CVD. In the 24 month (M) *post-hoc* analysis of the H2304 study, everolimus (EVR) with reduced tacrolimus (rTAC) or tacrolimus withdrawal (TAC-WD) provided adequate immunosuppression, improved renal function and reduced the incidence of major adverse cardiac events (MACE) compared with standard TAC (TAC-C). Here we present the *post-hoc* analysis of the CVD risk at 36M post LTx, from the randomized H2304 extension study.
Methods: H2304 is a 24M, randomized, open-label, multicenter study in which LTxRs on day 30 post-Tx were randomized to receive either EVR + rTAC ($n = 245$), EVR + TAC-WD ($n = 229$) or TAC-C ($n = 242$). After the core study, LTxRs were followed up for additional 12M. Renal function was measured by estimated glomerular filtration rate (eGFR) using the four-variable Modification of Diet in Renal Disease (MDRD4) formula. Adverse events (AEs) associated with MACE (ischaemic heart disease, cardiac failure, sudden death and ischaemic stroke) were used to determine the CV risk of this extension study population.
Results and Conclusions: Of the 716 randomized LTxRs, 282 were followed up till M36. At M36, eGFR values for TAC-WD, EVR + rTAC and TAC-C arms were 86 ± 27.4, 85.2 ± 30.5 and 70.8 ± 22.9 ml/min/1.73 m^2. The cumulative incidence of MACE was lower in the TAC-WD arm ($n = 3$; 15.6/1000 patient-years [PY]) compared with EVR + rTAC ($n = 8$; 22.5/1000 PY) and TAC-C ($n = 13$; 59.8/1000 PY) arms. The risk of MACE was also significantly lower ($P = 0.0105$) in the TAC-WD arm compared with the TAC-C arm. This M36 follow-up *post-hoc* analysis suggests that compared with TAC-C, EVR facilitated reduction or withdrawal of TAC, provides better renal function and is associated with lower incidence of MACE.

PV013 FACTORS INFLUENCING INTRA- AND EXTRA-HEPATIC RECURRENCE AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Introduction and Background: Tumor recurrence is the most frequent cause of death after liver transplantation (LTX) for hepatocellular carcinoma (HCC). To identify factors influencing intra- and extra-hepatic recurrence, we reviewed patients treated at our department from 1995 to 2014.
Methods: Our tumor register provided data of 146 consecutive patients on age, sex, Child stage, AFP, tumor diameter, number of tumors, venous invasion on histological definitive examination (VI), Milan-, BCLC and Duvoux-score, and time and location of recurrence. We differentiated between intra-hepatic (within the liver ± distant metastases) and extrahepatic (distant metastases only) recurrence (IHR and EHR, respectively). For multivariate analyses a COX-model was used.
Results and Conclusions: After a median follow-up time of 45 (3-148) months after LTX, 15 patients had IHR, 28 had EHR. The respective cumulative 10 year recurrence rates (10-Y RR) were 11 ± 3%, and 23 ± 4%. 10-Y RR for TR were statistically significantly influenced by Milan-, BCLC- and Duvoux-Score ($P = 0.013$, 0.045, and <0.001, respectively), number of tumors ($P = 0.002$), AFP-level >100 ng/ml ($P = 0.018$), and VI ($P < 0.001$). 10-Y RR for EHR followed the same pattern. For IR, we did not see a statistically significant difference in 10-Y RR for Milan, AFP and BCLC-score.

Venous invasion, Milan-, BCLC and Duvoux-score were included in a COX model. Only Duvoux-score and VI proved to be of independent influence on 10-Y RR for TR ($P = 0.013$, HR 2.920; $P < 0.001$, HR 3.896; respectively). The same factors influenced 10-Y RR for EHR ($P = 0.022$, HR 3.602; $P = 0.002$, HR 4.128; respectively). For IHR only VI independently influenced 10-Y RR ($P = 0.031$, HR 3.744).

In our series venous invasion was the most important factor influencing recurrence.

PV014 LONG TERM QUALITY OF LIFE AFTER COMBINED PANCREAS-KIDNEY TRANSPLANTATION

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Introduction and Background: As many other chronic diseases, type 1 diabetes has a direct impact on the quality of life. The present study investigates the influence of simultaneous pancreas-kidney transplantation (SPK) on the quality of life of patients with type 1 diabetes.
Methods: The health related quality of life was measured retrospectively with the Short Form Health Survey (SF 36) in 146 patients (65f:81 m, mean age: 51.9 ± 8.5) after successful pancreas-kidney transplantation and 51 patients (23f:28 m, mean age: 45.7 ± 8.1) on the waiting list. Quality of life was compared between the two groups and the influence of other variables (duration of diabetes, duration on dialysis, gender, age, comorbidities) on quality of life was included. The patients that underwent transplantation had a mean duration of diabetes of 31.3 ± 7.7 years and a mean time on dialysis of 26 ± 24 months, the patients on the waiting list had a mean duration of diabetes of 30.9 ± 8.7 years and a mean time on dialysis of 33.9 ± 36.5 months.
Results and Conclusions: Comparing the two groups, the physical and mental health summary scales of the quality of life showed significantly better results in the group of patients with a successful transplantation than in the group of patients on the waiting list ($P < 0.01$). After transplantation, there was a highly significant improvement in physical functioning, general health perceptions, social functioning, vitality and mental health ($P < 0.001$). Male patients of both groups showed significantly less physical pain, more vitality and a better mental health. Compared with German norm data, the transplant patients had a similar quality of life to the group of patients aged 61 to 70. A tendency towards better results in those patients within a shorter postoperative time span after transplantation could be seen.

Overall there is a significant increase in health-related quality of life in patients after successful combined pancreas-kidney transplantation.

PV015 LONG-TERM OUTCOME AFTER COMBINED KIDNEY-PANCREAS RECIPIENTS WITH MINIMIZED IMMUNOSUPPRESSION: A SINGLE CENTER REPORT

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Introduction and Background: We retrospectively analyzed long-term pancreatic and renal graft function, patient and graft survival and major complications after combined pancreatic-kidney transplantation (SPK) and Tacrolimus (Tac) or Cyclosporine A (CyA) monotherapy.
Methods: Between 1979 – 2015 performed at our center, 7 out of 489 SPKs patients were converted to Tac ($n = 6$) or CyA ($n = 1$) monotherapy in response to hematologic side effects ($n = 6$) or biopsy-proven BK-nephropathy ($n = 1$). Prior to monotherapy, patients were treated with Tac plus MMF ($n = 5$) or Tac plus Rapamycine ($n = 1$, study) or Tac-monotherapy (study, converted to CyA due to idiopathic thrombopenia), respectively, for a period of 62.1 (30-144) months (mean).
Results and Conclusions: At 133 (48-205) months all patients are alive with a stable pancreatic and renal function (mean creatinine 1.7 mg/dl ± 0.7 SD, blood glucose 97.1 mg/dl ± 12.2 SD, HbA1c 5.3% ± 0.3 SD, C-peptide 4.2 ng/l ± 2.1 SD, Tac-/CyA -level 5.6 ± 1.8 SD / 107 ng/ml).All major complications (urosepsis, incisional hernia, portal vein thrombosis, bleeding telangiectasia of graft duodenum, idiopathic portal hypertension, mild acute rejection, idiopathic thrombopenia, $n = 1$ each) were controllable. In one patient a biopsy proven acute vascular rejection (at month 33 within Tac-monotherapy, 155 month post transplant, C4d negative) was treated by adding MMF (discontinued after 6 weeks due to leucopenia and diarrhea) plus prednisolone (discontinued after 5 weeks for severe skin dystrophy). No antibody mediated rejection was observed. The most recent DSA screening was negative in 2 patients and is missing for logistic reasons in 5.
Conclusion: Late after SPK, Tac-/CyA monotherapy seems to be feasible in patients suffering from side effects of non-CNI immunosuppressants. Cautious dose adjustments, careful trough level monitoring and particular attention to strict adherence to the drug treatment may be particularly relevant in this context.

PV016 PREDICTORS AND PROTECTORS OF DONOR SPECIFIC ANTIBODIES AFTER LIVER TRANSPLANTATION

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Introduction and Background: Donor specific antibodies (DSA) developed as a risk factor after liver transplantation (LT) for complicated processes. Monitoring of DSAs is not yet standardized neither is the therapeutic procedure in case of humoral graft damage. This analysis wants to define factors that predispose patients for the development of DSAs after LT.
Methods: We established a database collecting clinical and demographic data of 400 liver transplant recipients receiving aftercare in the liver transplant unit of the university hospital Essen. Antibody-detection was performed by using Luminex single antigen beads and a mean fluorescence intensity (MFI) value of more than 500 was considered positive. For statistical analysis we employed SPSS software. A p-value less than 0.05 was considered statistically significant.
Results and Conclusions: The indication for liver transplantation is associated with DSAs. Patients who received LT due to an autoimmune liver disease developed DSAs significantly more often than patients with any other indication (29.3%; $P \leq 0.022$). Patients who receive LT due to a hepatocellular carcinoma (HCC) have a significantly lower risk to develop DSAs: of 79 patients with HCC only 6 (7.6%) developed detectable DSAs ($P \leq 0.002$). The risk to develop DSAs increases significantly 8 years after LT ($P \leq 0.005$). Interestingly, significantly less patients (10.6%; $P \leq 0.025$) who receive an mTor-Inhibitor-based immunosuppressive regimen do develop DSAs after LT compared to patients receiving a calcineurin-inhibitor (CNI) –based immunosuppressive therapy (43.1%).

Potentially due to a certain immunologic predisposition, patients with autoimmune liver diseases have a higher risk for the development of humoral graft damage and need a closer monitoring for DSAs. Immunosuppression with an mTor -inhibitor does obviously have a protective effect on DSA development and may be preferred for immunosuppression in those patients with a higher risk.

PV017 GRAFT TOLERANCE AND IMMUNOLOGICAL CONSEQUENCE FOLLOWING A COMBINED THI / CERTICAN® SUBSTITUTION AFTER LIVER TRANSPLANTATION IN THE RAT: A NOVEL IMMUNOSUPPRESSANT DRUG

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Introduction and Background: The allograft rejection (AR) has generally been considered a T-cell-dependent immune process. It is known that lymphocyte regress after transplantation depends on sphingosine 1-phosphate (S1P) receptor-1. Treatment with 2-Acetyl-4-tetra-hydroxybutyl imidazole (THI), a potentially immunosuppressant drug, inhibits the S1P-degrading enzyme and plays a fundamental role in the immune response. The aim of this experimental study is to evaluate the protective effects with mono-therapy after LTx in a rat model, or Certican®-combined THI treatment of the recipients. An understanding of this preconditioning of the allograft is essential for the design of therapeutic strategies as well as an improvement of survival after LTx for recipients with relevant immunosuppressant toxicity.
Methods: Orthotopic arterialised LTx in a rat model. The recipients are divided into 4 groups: group I (controls without THI or Certican® pre-/treatment/ immunosuppression of the recipients, $n = 6$); group II (immunosuppression of the recipients with high-dose Certican®, $n = 10$); group III (pre-/treatment of the recipients with THI, $n = 10$); group IV (pre-/treatment and immunosuppression of the recipients with low-dose Certican® and day 0-14 after LTx with THI, $n = 10$).
Results and Conclusions: Our preliminary data (histopathological findings and FACS) with application of a single THI-injection 60 min before LTx show a significant decrease of CD4 + /CD8 + populations of the T-lymphocytes in the recipients' peripheral blood and liver allograft. These results indicate that lymphopenia in the peripheral blood compartment is caused by a rapid sequestration after THI treatment, and gives credence to the theory that the reduction of T-lymphocytes with THI alone or in combination with low-dose Certican® before reperfusion will prevent or reduce acute rejection episodes in liver allografts.

The study is of considerable interest as it draws attention to the modulation of immune function after solid organ transplantation.

PV019 HUMAN *EX-VIVO* LIVER MODEL FOR ACETAMINOPHEN-INDUCED LIVER DAMAGE

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Introduction and Background: Acute liver failure (ALF) is a condition with loss of nearly complete liver function after severe damage which may result in the need for liver transplantation. One reason for ALF is the overdose of drugs like acetaminophen (APAP). Reliable test systems to identify hepatotoxicity are essential to study the mechanism of liver damage of known drugs and to predict unexpected drug-related liver injury of new drug candidates.
Methods: We established a human-based ex-vivo liver model able to keep hepatic functionality for up to 30 h and investigated drug-induced liver injury using APAP as model substance. Hourly samples from the perfusate were taken for measurement of general metabolism and clinical parameters. Liver function was assessed by clearance of indocyanine green (ICG) at 4, 20 and 28 h. APAP was applied after 8 h of perfusion with 6.5 mg/g of deployed liver tissue.
Results and Conclusions: Six pieces of untreated human liver specimen maintained stable liver function over the entire perfusion period. Three liver sections incubated with low-dose acetaminophen revealed strong damage, with ICG half-lives significantly higher than in non-treated livers after 20 h of perfusion ($P < 0.005$). Four liver sections revealed weak damage with significantly higher ICG half-lives after 28 h of perfusion ($P < 0.05$). Thus, this model allows for investigation of hepatotoxicity in human liver tissue upon applying drug concentrations relevant in humans and reflects well the inter-individual differences upon drug response observed in patients.

PV020 IMMUNOSUPPRESSIVE DRUGS FOR APPLICATION IN HEPATOCYTE TRANSPLANTATION - *IN VITRO* STUDIES USING PRIMARY HUMAN HEPATOCYTES

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Introduction and Background: Hepatocyte transplantation is of large potential as an additional treatment modality for certain liver diseases. However, insufficient engraftment and long-term acceptance of cellular allografts remain major challenges and still hamper broad clinical application. Aim of this study thus was to investigate whether i) immunosuppressive drugs known from solid organ transplantation show similar effectiveness for suppression of the immune response induced by primary human hepatocytes (PHH) and ii) isolated PHH are vulnerable to toxicity induced by these immunosuppressive agents potentially hampering cell engraftment in vivo.
Methods: PHH were isolated from resected liver specimens using a 2-step-collagenase perfusion technique. Adherent PHH were then co-culture with allogenic lymphocytes in terms of a mixed lymphocyte hepatocyte culture (MLHC) to characterize the immune response induced. Lymphocytes were labeled with PKH-26 to determine proliferation via flow-cytometry. MLHC was performed in the absence and presence of Cyclosporin, Everolimus, Belatacept and methylprednisolone (incubation time of 10 days). In addition, metabolic activity of PHH was assessed using the MTT-assay.
Results and Conclusions: Allogenic PHH induce a predominantly $CD4^+$ T-cell response in vitro. The immune response is well susceptible to suppression by Cyclosporin, Everolimus as well as Belatacept, whereas addition of methylprednisolone resulted only in minor reduction of T-cell proliferation. Cyclosporin, Belatacept and methylprednisolone had no significant inhibitory effects on metabolic activity of PHH in vitro as compared to controls. However, application of Everolimus significantly reduced the metabolic activity of PHH. In conclusion, Cyclosporin, Everolimus and Belatacept seem effective immunosuppressive drugs concerning alloreactivity in MLHC, nonetheless, Everolimus might turn out disadvantageous concerning cell engraftment and proliferation in vivo.

PV021 PERI-OPERATIVE ORGAN PERFUSION WITH ATG-FRESENIUS RESULTS IN IMPROVED GRAFT FUNCTION IN CLINICAL LIVER AND KIDNEY TRANSPLANTATION

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Introduction and Background: The use of marginal donor organs with the consequences of higher risk of unfavorable transplantation (Tx) outcome has become reality. In order to improve marginal allograft outcome, machine perfusion of solid organs has regained attention. As antithymocyte globulin (ATG) has been demonstrated to reduce I/RI, we hypothesize that pre-operative perfusion with ATG may be beneficial in reducing I/RI-related inflammation.
Methods: We performed a randomized controlled clinical trial involving 30 liver (LTx) and 50 kidney recipients (NTx) at the Innsbruck Medical University. Primary endpoints were defined as graft and patient survival after 7 days and one year; secondary endpoints were defined as initial graft function, presence of acute rejection, and clinical parameters. Prior to implantation organs were perfused and incubated for 5 min. with ATG-Fresenius ($n = 24$ NTx; $n = 16$ LTx) or saline.
Results and Conclusions: No significant differences were observed regarding donor and recipient characteristics between ATG perfused (AP) and control perfused (CP) organ recipients. During the early hospitalization phase, 16 out of 26 CP-NTx patients required dialysis during the first 7 days post Tx, whereas only 10 out of 24 AP-NTx patients received dialysis (P = n.s.). AP-NTx recipients illustrated clearly better graft function until day 15 post Tx reflected by lower creatinine and urea levels. This result was more evident in younger AP-NTx recipients (<55 years) compared with aged AP-NTx (≥55 years) patients ($P = 0.049$ at day 7 post Tx) – an effect which was not observed for CP-NTx patients. This result was further confirmed for young AP-LTx compared to CP-LTx patients reflected by reduced gamma-GT levels at day 10 post Tx ($P = 0.034$). Moreover, AP-perfused liver biopsies illustrate lower levels of CRP compared with CP livers post reperfusion ($P = 0.02$). We present here the first clinical study on peri-operative organ perfusion with ATG suggesting an age-dependent effect independent from the organ transplanted.

PV022 EARLY HCC IN COMPENSATED CIRRHOSIS SHOULD BE RESECTED IF POSSIBLE: A META-ANALYSIS OF TRANSPLANTATION VS. RESECTION

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Introduction and Background: Transplantation and resection remain the only curative treatments with acceptable long-term survival for HCC. In general, transplantation reaches better disease-free- and overall-survival by removing the precancerosis, thereby preventing de-novo occurrence. In light of the scarcity of post-mortal livers for transplantation however, effective strategies for primary treatment, bridging-to-transplant and organ preservation need to be defined.

In here we present the results of a meta-analysis of all studies comparing transplantation (LTx) and resection (RES) for early HCC.
Methods: A prospective search of Medline, PubMed, and EMBASE (OvidSP) was performed to identify relevant publications. Subgroup analysis was performed for studies conducting an intention-to-treat analysis (ITT) and tumors that were deemed resectable and transplantable (early-HCC). Relative treatment effects after 1, 3 and 5 years were reported as Odds-ratio (OR) of overall survival.
Results and Conclusions: Altogether 50 studies with 13196 patients were included in the analysis. Of these patients 7471 underwent resection and 5725 had a liver transplantation. Results after RES and LTx of early-HCC were similar after 1 and 3 years (OR 1.25; $P = 0.41$ and 0.80; $P = 0.36$ respectively). At 5 years of follow-up LTx significantly outperformed RES. In the ITT-Analysis however, RES showed significantly better results after 1 year (OR 1.36; $P = 0.005$). At 3-years results were similar and at 5 years again LTx showed better results (OR 0.89; $P = 0.51$; OR 0.61; $P < 0.001$).

In conclusion this shows that resection of small early HCCs is accompanied with an excellent short-term survival. Therefore, patients who could either be transplanted or resected would greatly benefit from resection as definitive or possibly a bridging-to-transplant treatment.

PV023 ENDOTHELIAL DYSFUNCTION MEASURED BY FLOW MEDIATED DILATATION IN PATIENTS ON THE WAITING LIST AND AFTER LIVER TRANSPLANTATION AS SURROGATE MARKER FOR CARDIOVASCULAR MORTALITY

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Introduction and Background: Cardiovascular events are a frequent cause for mortality after liver transplantation (LT). Patients on the waiting list suffering from liver cirrhosis (LC) show a hyperdynamic circulation compared to healthy subjects. Flow Mediated Dilatation (FMD) is the best non-invasive technique to assess endothelial function (ENF) by inducing a reactive hyperemia via temporary arterial occlusion and measuring the resultant relative increase in blood vessel diameter via ultrasound. Reduced vascular response on endothelial stimulation correlates with an inferior prognosis.

Aim of this work is to validate FMD and identify prognostic endothelial markers during evaluation for LT.

Methods: We investigated ENF via FMD during LT-evaluation in 100 LC patients. Cardiovascular status was assessed and FMD-measurements were correlated with patient characteristics and parameters of circulation, heart and liver function. Results were compared to an age- and BMI-matched healthy control (HC) cohort. LC patients who underwent LT were followed up prospectively 3 and 12 months after LT including FMD measurements.

Results and Conclusions: In total, 74% of LC patients showed altered FMD-values compared to the HC cohort (average FMD in LC at evaluation = 12.9% vs. FMD in HC cohort = 8.7%; $P < 0.05$). There was a positive correlation between FMD and Child-Pugh Score ($P = 0.008$). Furthermore, FMD negatively correlated with the mean arterial pressure ($P = 0.003$) and serum albumin levels ($P = 0.014$) at evaluation.

Until April 2016, 15 of 100 LC patients were transplanted and were alive 3 months after LT. FMD was increased at 3 months (average FMD = 16.8%) compared to FMD at baseline evaluation (average FMD = 14.5%) of these patients ($P < 0.05$).

FMD-measurement correlates with the stage of LC. Further studies are necessary to validate FMD as a non-invasive test for cardiovascular mortality after LT.

PV025 INFLUENCE OF PREFORMED DONORSPECIFIC HLA-ANTIBODIES ON KIDNEY TRANSPLANTATION - FIRST RESULTS OF A MULTICENTER RETROSPECTIVE STUDY

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Introduction and Background: HLA-specificities against which antibodies are detected by the classic complement-dependent cytotoxicity assay (CDC) are routinely avoided in the allocation of kidney allografts. Since many years, more sensitive methods allow the diagnosis of additional antibodies only detectable in solid-phase assays. The prognostic value of these antibodies, however, is still unclear. The current recommendations of the German Society of Immunogenetics (DGI) recommend that HLA-antibodies with median-fluorescence values (MFI) of less than 3000 in single antigen testing should not be assigned as unacceptable antigens for kidney transplantation.

Methods: All kidney transplantations from the participating centers performed between 2012 and 2015 were evaluated retrospectively. The specificities of HLA-antibodies from pretransplant sera (both sera from the quarterly antibody screening as well as sera drawn immediately prior to transplantation) were compared with the HLA typing of the transplanted kidney to determine preformed donor-specific antibodies (DSA). The outcome of kidney transplantation will be compared for the following three groups of patients: (1) patients without preformed DSA, (2) patients with preformed DSA with MFI-values of less than 3000 in single antigen testing, and (3) patients with preformed DSA with MFI-values of 3000 or more. The primary outcome parameter is the incidence of acute antibody-mediated rejection in the first 180 days after transplant.

Results and Conclusions: At the time of abstract submission, 2611 patients from 13 transplant centers have been included in the study. 216 patients (8%) had donor-specific HLA-antibodies (DSA) which had been detected prior to transplantation. 100 of these patients (4% of all patients) had preformed DSA with MFI-values of 3000 or more. The proportion of transplanted patients with preexisting DSA was different between centers and ranged from 2% to 22%. Data about transplant outcome is not available yet, but shall be presented at the meeting.

PV026 REJECTION OF HUMAN KIDNEY ALLOGRAFTS ACCORDING TO BANFF CLASSIFICATION IS ASSOCIATED WITH A CHEMOKINE-ENRICHED PROTEIN MICROENVIRONMENT IN BIOPSY TISSUE

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Introduction and Background: Expression profiling efforts of biopsy tissue after kidney transplantation indicate that rejection can be defined by distinct signatures. Based on pathological evaluation (BANFF) as T cell-mediated (TCMR), AMR or borderline rejection, we hypothesized that the presence of immune cells within the graft would be associated with a distinct cytokine milieu. Therefore, we determined the protein microenvironment in kidney biopsies and correlated cytokines and chemokines with pathological staging.
Methods: From our protocol biopsy program, 37 snap-frozen kidney biopsies were obtained from transplant recipients ranging from 2 months to 20 years after Tx with ethical approval, informed consent. Protein lysates of capsule, cortical and medullary biopsy regions were analyzed for 50 cytokines, chemokines using multiplex protein arrays. Histopathological evaluation of was performed according to BANFF criteria (14 unsuspicious, 4 TCMR, 5 borderline, 14 AMR).
Results and Conclusions: The protein microenvironment differed significantly between capsular, cortical and medullary kidney regions even in unsuspicious biopsies. In contrast, pro-inflammatory cytokines like IL-6, IL-8 (CXCL8), IFN-g, TNF-a were very low and did not differ between unsuspicious and rejection biopsies. However, significantly higher concentrations of chemokines like CXCL9, 10, CCL5, growth factors, i.e. HGF were detected in cortical and medullary biopsy regions of the rejection group (all $P < 0.01$).

The protein microenvironment of kidney biopsies histologically classified as rejection differs significantly from unsuspicious renal tissue with respect to the chemokine but not the cytokine milieu. Thus, certain chemokines like CXCL9, 10 confirm their qualification as biomarker candidates also at the protein level while typical T cell-derived cytokines seem to perform rather poorly as biomarkers.

PV027 *DE NOVO* DONOR-SPECIFIC HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION ARE CORRELATED WITH THE NUMBER OF PREDICTED INDIRECTLY RECOGNIZABLE EPITOPES

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Introduction and Background: *De novo* donor-specific HLA antibodies (DSA) have been recognized as being the leading cause of late renal allograft failure. *De novo* DSA posttransplant result from HLA mismatches under the impact of inadequate immunosuppression. Determinants of DSA specificity are generated via the indirect allorecognition pathway. We investigated the relevance of predicted indirectly recognizable HLA epitopes (PIRCHE) to predict the development of *de novo* DSA following kidney transplantation.
Methods: A total of 2787 consecutive kidney transplants performed between 1995 and 2015 have been analyzed. All patients had no DSA prior to transplant as detected by solid-phase immunoassays. Posttransplant *de novo* DSA were detected by the Luminex® single antigen assay. HLA epitope mismatches were determined by both the Matchmaker and PIRCHE approach. The count of epitope mismatches were correlated in uni- and multivariate analyses with renal allograft survival and the incidence of *de novo* DSA.
Results and Conclusions: The PIRCHE score moderately predicted death-censored 10-year renal allograft survival. However, the predictive value of PIRCHE scores >9 for development of DSA was statistically significant ($P < 0.001$). When analyzing the predicted impact of a high or low PIRCHE score on DSA development stratified according to the degree of antigen mismatch at each HLA locus a clear differentiation could be revealed for HLA-DR and DQ and to a lesser extent also for HLA-A and B. Almost no effect could be revealed for HLA-C. In a multivariate cox regression analysis adjusted for antigen mismatch and Matchmaker epitopes the PIRCHE score could be identified as independent risk factor for *de novo* DSA. PIRCHE score independently from antigen mismatch and Matchmaker epitopes could be revealed as having a strong predictive value for *de novo* DSA. Therefore, the PIRCHE score could help to identify acceptable mismatches with relatively reduced risk for development of *de novo* DSA and thus improve long-term renal allograft survival.

PV028 ABO BLOOD GROUP INCOMPATIBILITY HAS AN IMPACT ON T CELL FLOW CYTOMETRY CROSSMATCH RESULTS

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Introduction and Background: The flow cytometry crossmatch (FCXM) appears as more sensitive than a conventional lymphocytotoxic crossmatch. This study focuses on the impact of ABO blood group incompatibility on FCXM results prior to living donor kidney transplantation.
Methods: We analyzed 29 ABO incompatible donor-recipient pairs (73 data sets, i.e., on average 2.5 tests per pair) prior to kidney transplantation. As a control group, 89 ABO compatible pairs (175 data sets) were included. All donor-recipient pairs were negative for lymphocytotoxic crossmatches of T and B cells.
Results and Conclusions: Recipients with blood group O (A to O and B to O) displayed significantly ($P < 0.05$) higher T-FCXM results than those with blood group A and B (A to B, B to A and AB to A), respectively. Furthermore, donor-specific T-FCXM responses (delta MFI values) were significantly higher ($P < 0.05$) in all ABOi groups than in the ABO compatible group (ABOi recipient with blood group O: 32 ± 6; with blood group A: 19 ± 7; with blood group B: 7 ± 4; with ABO compatibility: 3 ± 2, resp., data represent mean $\pm$ SEM). Consistent with the T-FCXM results donor-specific isohemagglutinins (IgG titers) were significantly higher in recipients with blood group O vs. A, both prior to rituximab treatment and plasmapheresis/immune adsorption ($P = 0.004$) and immediately prior to kidney transplantation, i.e., after rituximab and antibody-depleting therapies ($P = 0.04$). As expected, IgG titers prior to rituximab treatment and prior to transplantation were significantly correlated ($r = 0.40$, $P = 0.04$). IgM titers of donor-specific isohemagglutinins yielded similar results. Recipients with blood group O vs. A displayed significantly higher titers prior to rituximab treatment and prior to transplantation ($P = 0.02$ each). In conclusion, reference values for the T-FCXM have to be re-assessed prior to ABO incompatible transplantation. The mechanism leading to increased T-FCXM results needs to be further elucidated.

PV029 GROWTH HORMONE RELEASING HORMONE (GHRH) AGONIST ATTENUATES IMMUNOSUPPRESSION RELATED NEGATIVE EFFECTS ON ISLET GRAFTS

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Introduction and Background: Following islet transplantation, a progressive islet loss is seen in the majority of patients. This decrease in graft function is in part resulting from adverse effects of immunosuppressive agents. The current protocols include a glucocorticoid-free combination of calcineurin-inhibitors (CNI), mTOR-inhibitors and Mycophenolate (MMF). In this study we aimed to investigate the impact of MMF and Everolimus on islet proliferation and functional capacity *in vitro* using adult rat islets. In addition, we sought to combine immunosuppressive agents with a growth hormone releasing hormone (GHRH) agonist that has been shown to promote islet proliferation, graft survival and function, which may help to reduce or even abolish potential negative effects of immunosuppression.
Methods: Rodent islets were isolated and purified according to standard protocol and maintained in culture for up to five days either alone or in the presence of MMF or Everolimus. GHRH agonist was added at previously tested concentration. Islets were analysed for viability and islet function (GSIR assay), immunohistochemistry was performed for apoptosis (TUNEL) and proliferation (Ki67).
Results and Conclusions: The viability after islet isolation was >90% and was maintained in the control group during the five day culture period with minor loss of islet mass. In contrast, the addition of either Mycophenolate or Everolimus caused a significant and progressive decrease in viability and function. This deleterious effect of the immunosuppressive agents was also reflected in a significantly increased percentage of apoptosis. The addition of GHRH agonist was able to abrogate these negative effects to nearly the level of

control islets and moreover, GHRH agonist treatment significantly induced beta cell proliferation as indicated by Ki67 immunohistochemistry.

In conclusion, we could show that immunosuppressive agents negatively impact on viability and function and this effect can be attenuated by the conditioning with a potent GHRH agonist.

PV030 INCREASED PRETRANSPLANT SERUM BAFF LEVELS ARE ASSOCIATED WITH REDUCED RENAL ALLOGRAFT SURVIVAL

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Introduction and Background: The essential function of BAFF is regulation of the survival and differentiation of B-cells. However, B-cells are involved in generation of donor specific antibodies (DSA) and contribute to the development of acute antibody-mediated rejection (AMR) in renal allograft recipients.
Methods: The objective of our retrospective single center study was to analyze pretransplant serum BAFF levels and to determine the association with preformed DSA, occurrence of AMR in the biopsy during the first post-transplant year and renal allograft survival. Soluble BAFF was measured by ELISA in 249 patients with end-stage renal disease undergoing renal transplantation between 2011 and 2012. Pretransplant anti-human leukocyte antigen (HLA) antibodies were identified by single antigen bead assay (Luminex™) in 25% of recipients, 15% of patients were HLA-donor specific antibody (DSA) positive.
Results and Conclusions: Pretransplant serum BAFF levels were significantly increased in patients with pretransplant HLA-DSA compared to pretransplant HLA-positive patients without DSA positivity (4112 $\pm$ 2609 vs. 2722 $\pm$ 2796 pg/ml, $P < 0.0001$) and compared to pretransplant HLA-negative patients (4112 $\pm$ 2609 vs. 2252 $\pm$ 1425 pg/ml, $P < 0.0001$). In ROC analysis a pretransplant serum BAFF cut-off of 2237 pg/ml was defined predicting presence of performed DSA with a sensitivity of 87.5% and a specificity of 62.5%. Patients with pretransplant serum BAFF levels >2237 pg/ml demonstrated significantly reduced 3-year allograft survival compared to patients with pretransplant BAFF below the cut-off (78% vs. 92%, $P = 0.0192$). Graft survival was significantly worse in patients with pretransplant BAFF >2237 pg/ml and histological signs of AMR during the first year posttransplant compared to the patients with high BAFF >2237 pg/ml who did not develop AMR posttransplant ($P = 0.0001$).

In conclusion, high pretransplant levels of BAFF are associated with reduced renal transplant survival and can be considered as a risk factor for AMR and renal allograft loss.

PV031 INDOCYANINE-GREEN FOR INTRAOPERATIVE LASER FLUORESCENCE ANGIOGRAPHY IN KIDNEY TRANSPLANTATION: PRELIMINARY EXPERIENCE AND DOSE FINDING

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Introduction and Background: Sufficient organ perfusion is vital for postoperative allograft function in kidney transplantation. Besides the surgeon's visual and tactile impression of the organ surface an objective method evaluating the quality of the graft's microperfusion is required. Laser fluorescence angiography with indocyanine-green (ICG) is an emerging tool for this purpose. Different ICG doses and settings were applied in prior publications.
Methods: This retrospective multicenter study was designed to evaluate the feasibility and dosing of ICG for intraoperative laser fluorescence angiography in kidney transplantation.

The Spy Elite system (NOVADAQ, Canada) was employed for qualitative and quantitative assessment of allograft microperfusion. ICG was administered systemically 5 min after reperfusion applying doses between 0.01 and 0.2 mg/kg body weight. Quantitative assessment was performed via the implemented SPY-Q Software.
Results and Conclusions: In this trial, 38 kidney recipients were included in 2 centers. There were no complications concerning ICG application. The generated curves showing ICG ingress and egress rates were not evaluable due to oversensing when doses exceeding 0.02 mg/kg body weight were applied.

Laser fluorescence angiography with ICG is a simple, safe and objective tool for the intraoperative quality control and evaluation of microperfusion in kidney transplantation. A dose of 0.02 mg ICG per kg body weight is recommended in order to ensure the quantitative assessment with SPYQ.

PV032 SURVIVAL BENEFIT FOR SENIOR PATIENTS RECEIVING A GRAFT WITHIN THE EUROPEAN SENIOR PROGRAM COMPARED TO PATIENTS ON THE KIDNEY WAITING LIST

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Introduction and Background: In recent years, the age of kidney donors and recipients has continuously increased. Therefore, the European Senior Program (ESP) allocation scheme was established by Eurotransplant in 1999 taking into account this demographic shift by allocating kidneys of donors >65 years to recipients >65 years. The results on patient outcomes comparing transplantation with younger and older grafts are controversial. Information on patient survival within ESP compared to patients remaining on the kidney waiting list is scarce.
Methods: All patients from the Transplant Center Cologne who had been waitlisted between 2000 and 2014 were included in the study. Patients transplanted between 2000 and 2014 within the ESP program were compared to patients transplanted within the regular Eurotransplant Kidney Allocation System (ETKAS).
Results and Conclusions: 1721 patients were included in this study. As expected, ESP patients showed a significantly shorter waiting time (38 $\pm$ 13 months) compared to ETKAS patients (78 $\pm$ 41 months). Waiting time for a transplant increased in the ESP program from 12 $\pm$ 2 months in the year 2000 to 59 $\pm$ 13 months in the year 2010, in ETKAS from 61 $\pm$ 38 months in 2000 to 78 $\pm$ 41 months in 2010. Patients transplanted in ETKAS showed a better survival than patients in ESP. Waitlisted patients >65 years showed a superior survival compared to ESP patients until 18 months after transplantation whereas after 20 months ESP patients showed a survival benefit. 24% of ESP patients showed organ loss during the study period compared to 18% of ETKAS patients. The benefit of a shorter waiting time in ESP compared to ETKAS for patients >65 years has significantly decreased from 2000 to 2014. ESP patients compared to patients on the waiting list show a survival benefit starting 18 months after transplantation. These findings will influence counseling of elderly patients in favor or against renal transplantation.

PV034 ACUTE POSTTRANSPLANT AHUS DUE TO A HOMOZYGOUS DELETION OF CFHR1/CFHR3 WITH CFH-AUTOANTIBODIES MANAGED BY A CNI-FREE REGIMEN WITH BELATACEPT AND ECULIZUMAB

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Introduction and Background: Acute renal graft failure may clinically present as atypical hemolytic uremic syndrome (aHUS), resulting from excessive activation of the complement cascade. Mutations of the complement coding genes predispose for development of aHUS. "Second hits" (e.g. drugs, pregnancy) commonly trigger the full-blown clinical picture. As calcineurin inhibitors (CNI) are considered one of these potential triggers, CNI-free regimens would be favorable. However, there is little experience regarding management of posttransplant aHUS and adequate long-term immunosuppression in these patients.
Methods: A 58-year old Caucasian female (ESRD of unknown origin) developed acute renal graft failure within days after transplantation, which clinically presented as aHUS (hemolytic anemia, thrombopenia, glomerular thrombotic microangiopathy). While complement analysis revealed autoantibodies versus complement factor H (CFH), genetic testing yielded a concomitant homozygous deletion of *CFH-related 1* (*CFHR1*) and *CFHR3*. Therapeutic management consisted of plasmapheresis, eculizumab (C5-inhibitor), and belatacept (blocker of T-cell co-stimulation) instead of CNI. Subsequently, renal graft function partially recovered to an eGFR of 32 ml/min for 18-month of follow up under continued administration of belatacept and eculizumab.
Results and Conclusions: This case describes the successful management of posttransplant aHUS using a CNI-free immunosuppressive regimen of eculizumab and belatacept. Recognition of predisposing risk factors, such as complement abnormalities, are crucial for development of tailored immunosuppressive regimens and long-term renal graft survival.

PV035 STRATEGY OF KIDNEY TRANSPLANTATION IN PATIENTS WITH ADPKD

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Introduction and Background: In Germany autosomal polycystic kidney disease (ADPKD) is one leading cause of end-stage renal disease. The surgical strategy of these patients in terms of performing a kidney

transplantation and its optimal timing remains controversial. Therefore, we analyzed pretransplant management and risk factors, as well as postoperative outcome and graft survival in our patients with ADPKD.
Methods: Our multivariate analysis ($P < 0.05$ is significant) includes renal transplant patients suffering from ADPKD and operated in our hospital between June 1995 and 2016. We discuss arguments and outcome for pretransplant nephrectomy, tumor incidence, postoperative graft function and complications after renal transplantation.
Results and Conclusions: 106 patients secondary to ADPKD underwent renal transplantation, 52% ($n = 55$) were male, with an average age of 57.2 years. 90% underwent bilateral nephrectomy before transplantation with serious complications in 2 patients. In 14% of the patients a renal cell carcinoma was found. 15% of the patients showed temporary blood pressure problems. Graft survival and long-term survival were not different in patients with or without nephrectomy before renal transplantation, but infectious complications were significant higher in patients without nephrectomy.

Bilateral kidney nephrectomy in ADPKD patients before transplantation is safe and recommended in terms of morbidity and graft function compared to posttransplantation nephrectomy of polycystic kidneys.

PV036 DIGITAL QUANTIFICATION OF MACROPHAGE ABUNDANCE IN A CROSS SECTIONAL STUDY OF TRANSPLANTED KIDNEYS

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Introduction and Background: Standardized markers based on quantitative/qualitative evaluation and localization of immune cell density in kidney transplant (KTx) biopsies may improve diagnostic accuracy.
Methods: Kidney biopsies were stained for macrophages using a CD68 antibody, scanned (Leica) and whole slide images were analyzed for immunopositively stained area using a digital approach (Definiens Tissue Studio). Results were obtained separately for cortex, medulla and extrarenal tissue. KTx biopsies were clinically indicated biopsies and samples from the Hannover Protocol Biopsy Program.
Results and Conclusions: CD68-positively immunostained area (% of the respective cortex, medulla, extrarenal area) was substantially higher in KTx ($n = 341$) vs. native kidney ($n = 131$) biopsies (cortex: 2.8 vs. 0.97, medulla: 2.71 vs. 0.71, extrarenal tissue: 1.92 vs. 0.71; $P < 0.001$). 40% of the studied KTx biopsies revealed rejection (borderline 15%, cellular 8%, humoral 7%, combined cellular and humoral 10%). Humoral and combined rejection were correlated ($P < 0.05$) with increased macrophage infiltration (cortex: no rejection 2.9%, borderline 2.1%, cellular 2.5%, humoral rejection 4.6%, combined rejection 6.2%). The density of macrophages correlated with the time between transplantation and biopsy ($P < 0.05$): Highest mean values ($P < 0.05$) were measured when post -transplant time exceeded 1 year (cortex: 5.6% compared to <1 year and >90 days (4.2%), <90 days and >8 days (1.7%), <8 days (1.6%); medulla: 5.9% compared to <1 year and >90 days (3.2%), <90 days and >8 days (1.9%), <8 days (1.8%)). Evaluation of IF/TA according to Banff 2013 consensus showed a significant increase of infiltrating macrophages with fibrosis progression (cortex: ci0: 1.6%, ci1: 4.7%, ci2: 6.6%, ci3: 7.5%; ct0: 3.7%, ct1: 2.6%, ct2: 6.6%, ct3: 7.5%).

The findings suggest that macrophages have an essential role in active rejection and chronic allograft injury. Digital morphological approaches may facilitate the characterization of immune cell-mediated kidney injury after KTx.

PV037 INDUCTION THERAPY IN LOW-RISK RENAL ALLOGRAFT RECIPIENTS – CAN WE SPARE IT TO AVOID INFECTIOUS COMPLICATIONS?

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Introduction and Background: The goal of induction therapy is to prevent acute rejection during the early period after kidney transplantation. However, it has been associated with complications such as post-transplant infections and malignancies. Considering a risk-benefit analysis we hypothesized that one might be able to avoid induction therapy in recipients at a low risk for acute rejection such as non immunized patients.
Methods: To proof our hypothesis we retrospectively analyzed 188 non-immunized renal transplant recipients who received an induction (IND) or no induction (NO) therapy. The maintenance triple therapy consisted of a calcineurin inhibitor (cyclosporin A or tacrolimus) MMF and steroids. Acute rejection (AR) episodes within the first year, infectious complications with special focus on BKV viremia, development of anti-HLA antibodies, graft survival as well as renal function assessed by creatinine levels were evaluated within a median follow-up of 3 ± 0.57 years.
Results and Conclusions: The rate of AR was significantly higher in patients of the NO as compared to IND group (31.63 vs. 18.89%, $P = 0.045$). More patients in the NO group tended to developed anti-HLA antibodies (25.26 vs. 16.92%, $P = 0.210$) and donor-specific anti-HLA antibodies (15.79 vs. 9.23%, $P = 0.228$). However, renal function was similar in both groups until 1 year after transplantation and to our surprise significantly worse in IND group thereafter. The rate of BKV viremia was lower by trend in the NO (5.50%) as compared to the IND group (8.90%, $P = 0.454$).

Induction therapy reduced the risk of AR in the first year, but did not improve long-term renal function. However it tended to increase the risk of infectious complications. Thus the use of induction should be adapted to the patients individual immunologic risk.

PV038 EFFICACY AND SAFETY OF THREE DIFFERENT TREATMENT REGIMEN IN *DE NOVO* RENAL TRANSPLANT PATIENTS: 5-YEAR FOLLOW-UP RESULTS OF THE HERAKLES TRIAL

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Introduction and Background: To compare safety and efficacy of 3 different immunosuppressive regimens at month (Mo) 60 after kidney transplantation (KTx).
Methods: 802 patients (pts) were included in this 1 year, prospective, open-label, randomized, controlled multi-center study with observational follow-up (FU) to Mo 60 post KTx. After induction therapy all pts received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3 Mo post KTx, 499 pts were randomized 1:1:1 to either a) continue standard CsA (100–180 ng/ml) + EC-MPS ($n = 166$) (STD) or convert b) to an everolimus (EVR)-based calcineurin inhibitor (CNI)-free regimen (with EVR 5–10 ng/ml) + EC-MPS ($n = 171$) or c) to a CNI-reduced regimen with EVR (3–8 ng/ml) + reduced CsA (50–75 ng/ml; $n = 162$). All pts continued on steroids according to centers practice. In total 77% of pts completed the FU period: 75% of STD, 84% of CNI-reduced and 84% of CNI-free group pts.
Results and Conclusions: During FU period to Mo 60 efficacy events from ITT were reported as follows: BPAR was reported in 13/165 (8%) STD, 13/171 (8%) CNI-free and in 12/161 (7%) CNI-reduced pts (p value =ns). 7 deaths (4%) occurred in STD, 4 (2%) in CNI-free and 9 (6%) in the CNI-reduced group. 7 (4%) graft losses were observed in the STD, 7 (4%) in the CNI-free and 3 (2%) in the CNI-reduced group. Composite failure (BPAR, death, graft loss, loss to FU) occurred in 38 (23%) STD, 35 (20%) CNI-free and in 36 (22%) CNI-reduced treated pts. eGFR (Nankivell; ITT, adjusted LS-Mean, LOCF) was significantly improved by +6.7 ml/min in favor of the CNI-free regimen at Mo 60 ($P < 0.001$). Safety profile did not differ between groups.
Conclusion: Mo 60 results from HERAKLES show that immunosuppressive regimens using EVR with reduced-dose or without CNI-exposure reflect an efficacious and safe therapeutic approach offering the opportunity for an individualized immunosuppression to minimize CNI-exposure.

PV039 THE "WEEKEND EFFECT" IN KIDNEY TRANSPLANTATION – A SINGLE CENTER STUDY

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Introduction and Background: The "weekend effect" describes increased adverse events and outcomes for patients hospitalized on weekends due to limited resources at hospitals and - in the context of renal transplantation (Rtx) - has also been shown to affect the organ discard rate of deceased donor kidneys.
Methods: We examined weekend-weekday differences in the outcome of 616 patients following RTx (brain dead donors) between January 2007 and December 2014 at our center. Patient and graft survival at 1 year (y) after Rtx, frequencies of delayed graft function (DGF, need for dialysis < 1 week post RTx) and biopsy proven acute rejections (AR) within the first year after RTx, as well as surgical complications requiring reoperation or interventional treatment after RTx were assessed.
Results and Conclusions: Of all 616 postmortal RTx, 442 (71.8%) were performed on weekdays (Monday-Friday) and 174 (28.2%) on weekends (Saturday/Sunday). 1y patient and graft survival were similar between weekend RTx and RTx performed on weekdays (97.7% vs. 96.7%, $P = 0.8$ and 93.5% vs. 93.1%, $P = 1.0$). Frequencies of DGF and AR were not different between both groups (25.3% vs. 25%, $P = 1.0$ and 22.6% vs. 21.1%, $P = 0.74$). Surgical complications (hemorrhagic, vascular, ureteral, lymphatic,

wound complications) occurred more often after RTx performed on weekends (35.1% vs. 26.5%, $P = 0.04$). Notably, cold ischemia times were lower in weekend RTx (10.3 ± 0.3 vs. 11.2 ± 0.2 h, $P = 0.03$).

In our cohort, a weekend effect was observed regarding surgical complications which, however, did not affect the patient and transplant outcome. The shorter cold ischemia times in weekend RTx might reflect an alertness of the challenges and difficulties in organ acceptance on weekends and the increasing strategies to extenuate this effect.

PV040 IMPACT OF COLD ISCHEMIA TIME ON CYTOKINES / CHEMOKINES IN VENA RENALIS BLOOD SAMPLES IMMEDIATELY AFTER REPERFUSION IN KIDNEY TRANSPLANTATION

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Introduction and Background: In addition to other causes, the duration of cold ischemia is hold responsible for the extent of the ischemia-reperfusion injury of the graft. We investigated if there are parameters which are correlated with the cold ischemia time (CIT), and accordingly allow conclusions about the quality of the graft.
Methods: In 82 patients, who received a kidney transplant at our hospital, the cytokines / chemokines Interleukin (IL) IL6, IL8, IL10, IL18, Interferon gamma-induced protein 10 (IP-10), Monocyte chemotactic protein 1 (MCP1) and Monokine induced by Gamma-Interferon (MIG) were measured using Multiplex analysis by Luminex bead technology. Immediately after beginning of reperfusion, the blood samples were obtained from the Vena renalis. The CIT was less than 10 h in 47 patients (group 1) and longer than 10 h in 28 patients (group 2). The third group consisted of 7 living donations (CIT < 2 h).
Results and Conclusions: The median values of the parameter levels of the patients in group 3 (living donation) are lower than the ones in groups 1 and 2. Due to the low sample size in group 3 a definite statement about the significance of this result is not possible. There were no significant differences among group 2 and 3.

In our study, the measured parameters show no correlation with the CIT. But it is interesting to note that the levels of proinflammatory cytokines in living donations are much lower than in postmortal donations. It can be assumed that other factors are responsible for this result and should be included in considerations.

PV041 THE IMPACT OF BLOOD PRESSURE VARIABILITY ON GRAFT SURVIVAL AND MORTALITY AFTER KIDNEY TRANSPLANTATION

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Introduction and Background: Elevated long-term blood pressure variability has been shown to be predictive of adverse outcomes in patients with chronic kidney disease. In kidney transplant recipients a negative correlation between endothelial function and short-term variability has been found. No data exist, however, for associations of visit-to-visit variability (long-term variability) and outcomes after kidney transplantation.
Methods: 877 patients who underwent kidney transplantation at the Charité-Universitätsmedizin Berlin and at the Universitätsklinikum Knappschaftskrankenhaus Bochum, Germany were included in this retrospective study. Patients were followed up for at least 12 months (up to 266 months) after transplantation. Visit-to-visit blood pressure variability over the first 12 months after transplantation (3 visits) and during the first 120 months after transplantation (7 visits) was calculated as the coefficient of variation (CV) = standard deviation (SD)/ mean blood pressure.
Results and Conclusions: Patients were categorized to those with low vs. high level of systolic CV at 12 months, defined by the median value (CV <5.6 and CV≥5.6%). After adjustment for gender, age and mean creatinine over the first 12 months the combined endpoint of death or graft loss did not differ between the two groups (HR (95% CI) = 1.1 (0.82–1.56), $P = 0.44$). No association was also found between patients with low and high systolic CV over 120 months ($P = 0.15$). Only primary graft function was associated with better outcomes after transplantation ($P < 0.001$).

Visit-to-visit blood pressure variability is not associated with mortality or graft loss after kidney transplantation in this retrospective analysis. The presence of primary graft function was predictive of better long-term outcomes after transplantation.

PV043 TREATING AORTIC VALVE STENOSIS IN KIDNEY TRANSPLANT RECIPIENTS – THINK ABOUT THE GRAFT NOT ONLY THE HEART!

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Introduction and Background: Surgical aortic valve replacement (SAVR) in kidney transplant recipients (KTR) with severe aortic stenosis (AS) is associated with high morbidity and mortality, especially due to cardiovascular and infectious complications, and an increased risk of postoperative kidney failure potentially leading to graft loss. Preliminary data from our center showed that transcatheter aortic valve implantation (TAVI) is safe and effective in KTR. However, long-term data on TAVI in KTR are still lacking.
Methods: We retrospectively analyzed all 40 KTR, in which aortic valve replacement was performed at our center between 2005 and 2015. We compared the outcome and follow-up of TAVI ($n = 20$) versus SAVR ($n = 20$) with respect to patient and graft survival. The decision for each treatment strategy was shared for every single case within the interdisciplinary heart team.
Results and Conclusions: Patient characteristics in both groups were comparable, with patients in the TAVI group tending to be older (69 vs. 65.5 years; $P = 0.06$). Mean duration of hospitalization in the TAVI group was 19 (11.5 to 21.75) days. Patients after SAVR had a significantly longer stay with 33 (21 to 62) days. After SAVR, there was a more pronounced SIRS (measured by CRP) and more frequent acute graft failure (45% vs. 89.5%; $P = 0.006$). Graft losses occurred without exception in the surgically treated group ($n = 7$). The 30-day mortality was 10% in both groups. However, the in-hospital mortality reached 25% in the SAVR group (TAVI 10%), indicating a more complicated course after surgery. 1-year survival after TAVI was 90%, compared to 69% after SAVR. Long-term follow-up showed comparable results after 5 years in both group (TAVI 58% vs. 52% SAVR). In KTR with severe aortic stenosis TAVI can be performed with good long-term results. Compared to SAVR, TAVI shows better short term results and, eminently important, leads to less graft loss. Anyway, careful treatment planning and risk stratification in this special population remains mandatory.

PV046 MACROPHAGE INVASION IN HEPATOCELLULAR CARCINOMA ASSOCIATES WITH RECURRENCE FREE SURVIVAL AFTER LIVER TRANSPLANTATION

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Introduction and Background: Tumor-associated macrophages (TAMs) promote tumor progression and have an effect on survival in human cancer. However, little is known regarding their influence on prognosis after orthotopic liver transplantation for de novo hepatocellular carcinoma (HCC).
Methods: We analyzed tumor specimens of HCC ($n = 33$) in hepatectomy specimens for distribution and localization of TAMs, as defined by expression of CD68. Abundance of TAMs was correlated with clinicopathologic characteristics, tumor recurrence and patients' survival after liver transplantation. None of the patients received neoadjuvant radio- and/or chemotherapy prior to transplantation. Statistical analysis was performed using SPSS software.
Results and Conclusions: Patients with high prevalence of TAMs in tumorous tissue of hepatectomy specimen showed significantly larger tumor nodules ($\rho < 0.05$). TAMs along with other established prognostic variables, such as T stage and lymphangiosis carcinomatosa were confirmed as independent prognostic variables in multivariate analysis regarding recurrence free survival (all $\rho < 0.05$).

In conclusion, our study provides first evidence that CD68 associates with clinicopathological parameters and survival following liver transplantation for HCC. CD68 might serve as a potential biomarker in HCC in the setting of liver transplantation, whereas further studies are needed to elucidate its functional role.

PV048 SIMILAR OUTCOME FOR (E)RLL AND FULL GRAFT LIVER TRANSPLANTATION - AN ANALYSIS FROM THE EUROTRANSPLANT LIVER FOLLOW-UP REGISTRY

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Introduction and Background: Split liver transplantation is an established technique to effectively increase the donor pool. Previously published data indicate a similar outcome of split and full graft liver transplantation (fgLTx). However, most of these data were on procedures where the two splits of the liver were transplanted in one center keeping cold ischemia times (CIT) as low as possible. In the ET area it is common practice that the (E)RLL is shipped from the splitting center to a second center. This results in prolonged CITs. We hypothesized that the combination of the splitting procedure and prolonged CITs affects the outcome of the (E)RLL compared to the full graft liver transplants.
Methods: Data on all LTx performed between 2007 and 2013 were retrieved from the ET Liver follow-up Registry ($n = 5351$). Data on $n = 5013$ (269 (E) RLL, 4744 full graft) Ltx could be included. A thorough statistical workup ensued.
Results and Conclusions: Cold ischemia times were significantly prolonged for split LTx ($P < 0.001$). The survival was not different between (E)RLL and full graft LTx. In the univariate analysis split liver transplants had a significantly higher risk for retransplantation ($P = 0.021$). For fgLTx the risk for death gradually and significantly increased with LabMeld-scores of >20. For (E)RLL LTx this effect was seen already with LabMELD scores of >14.

The outcome after (E)RLL and full graft liver transplantation is comparable with respect to survival. The risk of retransplantation seems higher after (E)RLL Ltx. The cold ischemia time has a significant impact on the overall outcome and may serve as a possible explanation for the higher retransplant rate.

PV051 VARIOUS METHODS OF EXTRACORPOREAL SUPPORT PRIOR TO LUNG TRANSPLANTATION – A BRIDGE TO SURVIVAL STRATEGY IN ULTIMATE RISK PATIENTS

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Introduction and Background: Lung transplantation (LTx) in patients bridged with extracorporeal membrane oxygenation (ECMO) was shown to be associated with relatively poor results especially in cases of mechanically ventilated patients. Only few reports from experienced centers presented reasonable outcomes of LTx in patients bridged to transplant with ECMO. The aim of our study was to present our institutional experience with various strategies of extracorporeal support as a bridge to LTx.
Methods: A total of 326 LTx were performed from 01/2010 to 03/2016 in our institution. Included were 31 patients (9.5%) from this cohort who were bridged to transplant using extracorporeal support. Strategies included were veno-venous (55%) or veno-arterial ECMO (16%), peripheral (16%) or central (6%) interventional lung assist (iLA), or a combination of them (13%).
Results and Conclusions: Four patients (13%) died on extracorporeal support prior to LTx, whereas 27 (87%) were successfully transplanted: 22 (81%) as a first time transplant and 4 (15%) as a redo transplant. The median age of the population was 33(25;41) years and 52% were female. Most patients had cystic fibrosis (55%) followed by pulmonary fibrosis (22%), pulmonary hypertension (16%), Ehlers-Danlos syndrome and bronchiectasis (3.5% each). The median duration of support was 10(6;17) days. Thirteen patients (50%) were non-intubated and self-ventilated during support. The median duration of mechanical ventilation after LTx was 318(140;574) hours, duration of ICU stay 18 (13;28) days and total hospital stay 38(32;67) days. Over the median follow-up of 364 (42;998) days 58% of the entire cohort and 68% of patients underwent first time LTx were alive and all patients remained free from bronchiolitis obliterans syndrome. Bridging to Ltx with extracorporeal support is an effective strategy in selected patients providing good postoperative outcome. Particularly avoiding invasive mechanical ventilation during support seems to be an important factor improving results.

PV052 IMPACT OF GASTROESOPHAGEAL REFLUX DISEASE ON GRAFT FUNCTION AFTER LUNG TRANSPLANTATION – RISK FACTORS, AETIOLOGY AND LONG TERM OUTCOME

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Introduction and Background: The incidence of Gastroesophageal Reflux Disease (GORD) in lung transplant (LTx) recipients has been previously reported to be very high. GORD is a risk factor for the development of chronic lung allograft dysfunction (CLAD).Its high prevalence after surgery might be related to preoperative incidence, vagal damage during surgery and/or immunosuppression. The aim of the study was to evaluate potential risk factors and aetiologies with particular focus on the impact of different transplant surgical techniques.
Methods: We retrospectively analysed data from consecutive lung transplant recipients who underwent impedance study postoperatively in our institution. Patients were considered GORD positive when number of total reflux episode was above 73 and or the total percentage time refluxing was above 2.1 at the impedance. Donor and recipients characteristic, peri, intra and postoperative variables were considered.
Results and Conclusions: Baseline characteristics (donor and recipient) did not differ between both groups. GORD was diagnosed in 107 patients (54.3%).Presence of GORD was associated with worse graft function in terms of lower FEV1 at 1 and 3 years ($77.14 \pm 20.75\%$ vs. $86.02 \pm 22.15\%$, $P = 0.03$; $70.87 \pm 22.26\%$ vs. $85.1 \pm 21.15\%$, $P = 0.053$) and more frequent episodes of at least grade A2 acute cellular rejection ($n = 20$, 20.6% vs. 4, 4.8%; $P = 0.002$).There was no difference observed in terms of the surgical approach (Clamshell vs. bilateral thoracotomy).The incidence of CLAD (defined as BOS) and the overall survival did not differ between both groups, however in both analysis, GORD positive patients showed a clear drop at 4 years after transplant. Our study showed the high incidence of GORD in lung transplant recipients which is associated with significant reduction in lung function tests in the mid- and long term after transplantation. Patients with GORD showed also worse graft function and more frequent episodes of acute rejection. However, no independent risk factor including different surgical approaches were observed for GORD.

PV054 CAN RESISTANCE TRAINING IMPROVE QUALITY OF LIFE AND MUSCLE STRENGTH IN A PATIENT WITH CONTINUOUS FLOW LEFT VENTRICULAR ASSIST DEVICE?

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Introduction and Background: Patients suffering from end-stage heart failure have limitations to exercise, which promote a muscular mass decline leading to a loss of physical constitution and quality of life (QoL). Even though left ventricular assist devices (LVAD) may improve hemodynamics and restore activity, there is rare knowledge about the effects of resistance training (RT) in LVAD-patients.
Methods: Hypothesizing that RT in LVAD-patients is practicable, counteracts frailty, increases the muscular mass and QoL, we observed one patient with terminal DCM and implanted LVAD practicing RT-exercises individually developed by a sports scientist and supervised by attending physicians 3 times weekly for a total of 5 months. At baseline and monthly thereafter, body stability and isometric maximum-strength measurements were obtained, as well as the six-minute walking distance (6MWD), spiroergometry, transthoracic echocardiography (TTE), the Minnesota Living with Heart Failure Questionnaire and laboratory parameters.
Results and Conclusions: Improvements of isometric maximum-strength especially in the lower extremity (+106.84% left /+89.70% right hamstrings;

+106.74% left /+81.72% right quadriceps, baseline vs. month 5; *Figure 1*) were found. 6MWD improved more than 20% during the study period (426 m at baseline to 494.3 m at 5 months). Laboratory parameters (nt-proBNP and hsTroponinT) remained at low levels throughout the observation time, corresponding to stable TTE-findings (TAPSE at baseline 15.3 mm vs. 12.8 mm at 5 months) and no major differences in stability tests. The subjective QoL improved markedly (30 points at baseline vs. 12 points at month 5). Summarizing, we provided evidence that specific RT in a LVAD-patient lead to an improvement of isometric maximum-strength in particular muscle groups. Furthermore, 6MWD and QoL showed an extensive increase whereas cardiac functional parameters remained stable. Concerning to our case report further studies are needed to evaluate RT in patients with LVAD regarding heath constitution and QoL.