POSTERS

INFECTIOLOGY

P01 FEASIBILITY OF ELBASVIR/GRAZOPREVIR FOR TREATMENT OF CHRONIC HEPATITIS C VIRUS INFECTION IN RENAL TRANSPLANT RECIPIENTS WITH IMPAIRED ALLOGRAFT FUNCTION

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Introduction and Background: Direct-acing antiviral agents are highly efficient treatment options for chronic hepatitis C virus (HCV) infection after renal allograft transplantation. Treatment options for patients with impaired graft function remain limited. Therefore, we assessed efficacy and safety of elbasvir/grazoprevir in chronic HCV- infected renal transplant patients with impaired allograft function.
Methods: Eleven renal allograft recipients with therapy-naïve HCV genotype (GT) 1a, 1b, or 4 were treated with the fixed dose combination of elbasvir/grazoprevir without ribavirin for 12 weeks. All recipients exhibited an impaired graft function with a glomerular filtration rate (GRF) < 60 ml/min/1.73 m² (MDRD equitation). Clinical data were retrospectively analysed for renal and liver function parameters. Patients were closely monitored for trough levels of immunosuppressive agents, viral load, laboratory values, and potential adverse effects.
Results and Conclusions: Seven patients (64 %) exhibited a rapid virologic response within 4 weeks (HCV GT1a, $n = 2$; HCV GT1b, $n = 5$). The other four patients achieved a virologic response within 8 weeks (HCV GT1b, $n = 3$, HCV GT 4 $n = 1$). Results for sustained virologic response at week 12 after the end of treatment are currently pending. Clinical measures of liver function improved substantially for all patients. Adverse events were scarce (arterial hypertension ($n = 8$), gastrointestinal symptoms ($n = 8$), fatigue ($n = 6$), headache ($n = 3$)). Impaired renal allograft function and proteinuria remained stable. Importantly, dose adjustments for tacrolimus were necessary for maintaining sufficient trough levels in a majority of patients. In conclusion, the described regimen appears to be safe and effective for recipients with impaired allograft function after renal transplantation and is a promising treatment option for eradicating HCV in this patient population.

P02 ACCIDENTAL TRANSMISSION OF HEPATITIS C (HCV) VIRUS FROM AN ORGAN DONOR TO FIVE TRANSPLANT RECIPIENTS: EARLY TREATMENT WITH DIRECT ACTING ANTIVIRALS SUCCESSFULLY PREVENTS HCV-INFECTION

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Introduction and Background: Limited data exist analysing transmission rates of Hepatitis C virus (HCV) and time course of HCV infection after solid organ transplantation. No data exist on the efficacy and outcome of an early-initiated treatment course with new direct acting antivirals (DAAs) directly after confirmed HCV transmission.
Methods: Clinical information of the HCV-positive organ donor and five recipients in five different transplant centres after accidental HCV transmission were collected. Sera from all recipients and the donor were tested for serologic and nucleic acid tests (NAT) of HCV infection before and 16 weeks post-transplant.
Results and Conclusions: The organ donor was a 55 years old woman who died due to subarachnoid haemorrhage. The donor did not belong to a HCV high-risk group. On day 4 of ICU stay donor received one unit of packed red blood cells. Routine serological testing for anti-HCV IgG at time of donation was negative. NAT for HCV was initially not performed.

All 5 transplant recipients were tested negative for anti-HCV IgG and had negative HCV-NAT before transplantation. All patients had detectable quantitative (q) HCV-NAT early post-transplant. Retrospective analysis revealed that the organ donor had low level HCV-RNA (17,700cop;genotype 1a) in the blood.

In 4 patients, a 12 weeks course of different DAA regimens was initiated after a median of 9.5 days with early viral response (EVR) at treatment week 4. The liver recipient had multiple postoperative complications and died due to septic shock. All other recipients had good graft function 16 weeks post-transplant and achieved a sustained virological response 4 weeks after end of therapy (SVR4).

HCV has a high transmission rate in solid organ transplantation with early active replication onset in the recipient. Early initiation of therapy with DAAs seems to effectively prevent chronic HCV infection.

P03 IMMUNE MONITORING-GUIDED TREATMENT OF A PEDIATRIC PATIENT WITH SEQUENTIAL GVHD, ACUTE REJECTION AND CMV INFECTION FOLLOWING LUNG TRANSPLANTATION

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Introduction and Background: A 17 year old patient with cystic fibrosis (HLA-A11+,CMV-) underwent bilateral sequential lung transplantation (donor: HLA-A32+,CMV+). Immunosuppression (IS) consisted of Tacrolimus, MMF and Prednisone. After uneventful 3 months, he developed histology-proven cutaneous GvHD treated successfully by withdrawal of MMF. He developed acute rejection treated by a steroid pulse. While lung function returned to normal, he developed CMV infection despite valganciclovir prophylaxis.
Methods: Frequencies of HLA-A32+ donor lymphocytes were measured by FACS. ELISpots were performed to detect allospecific (rejection vs. GVHD) and CMV-specific T cells. HLA-A2/NLV-pentamer staining was used for CMV-specific CD8+ CTL. Plasma cytokines were measured by multiplex assays.
Results and Conclusions: With development of skin GvHD, frequencies of 4% HLA-A32+ donor CD4+, CD8+ T cells, 5–8% B cells and 1–4% NK cells were detected for 2 weeks. Donor T, NK cells declined after MMF withdrawal, B cell frequencies remained stable. Simultaneously to improvement of GVHD, acute rejection developed, accompanied by significantly increased allo-A32-specific CD8+ T cells, which declined upon steroid pulse. Allo-HLA-A11-restricted T cells were found at low frequencies. Steroid pulse was accompanied by serological detection of CMV which induced HLA-A2/NLV specific CD8+ T cells producing IFN-g. CMV viremia disappeared with the emergence of CMV-specific CTL. Plasma levels of sCD25, IFN-g responded to IS alterations, to pulsed steroids with a transient drop.

Using specific immune monitoring tools, we could confirm clinical diagnoses of the patient. Frequencies of allo- or virus specific T cells, donor lymphocytes and plasma cytokine levels followed the clinical course of GVHD, followed by rejection followed by CMV infection. The modification of IS by using immune monitoring information resulted in a full recovery of the patient who is still asymptomatic several months after these complications.

P05 SAFETY OF DAA THERAPY REGARDING RENAL FUNCTION IN POST-LIVER TRANSPLANT PATIENTS INFECTED WITH HEPATITIS C AND A 100% SVR12 RATE - A SINGLE CENTER STUDY

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Introduction and Background: Direct acting antiviral (DAA) therapy of hepatitis c virus (HCV) infection is well established in patients with and without cirrhosis of the liver. Patients after liver transplantation with ongoing HCV infection often suffer from renal and hepatic impairment. A major concern when treating HCV patients after liver transplantation is the potential interaction of

DAA and immunosuppressive therapy that might result in decreasing renal function.
Methods: In this single centre study we analyzed clinical parameters of 18 HCV infected patients treated with DAA therapy after liver transplantation. The primary endpoints were change of renal function (GFR) and viral eradication 12 weeks after therapy (SVR 12). For secondary endpoints we investigated the influence of DAA therapy over time on transaminases, bilirubin, INR, non-invasive fibrosis measurement and MELD Score.
Results and Conclusions: 5 out of 18 patients treated with DAA suffered from renal impairment stage 2 and 7 out of 18 patients of renal impairment stage 3. Renal function at SVR 12 was neither influenced whether there was pre-existing renal impairment ($p > 0.5$), nor by the type of immunosuppressant ($p > 0.5$), nor the type of DAA regime ($p > 0.5$). All patients reached SVR12 regardless to their genotype or the type of DAA regime. In respect of secondary endpoints the type of immunosuppressant had no influence on renal function or SVR12 rate. The levels of transaminases and bilirubin declined rapidly as expected. 10 out of 18 patients already suffered from cirrhosis or liver fibrosis greater than F3 in non-invasive measurement before initiation of treatment. Even in this short period of time single point acoustic radiation force impulse imaging (ARFI) improved in 9 patients ($p = 0.012$). In conclusion, DAA-therapy in liver transplant patients was effective and safe in this single centre real life cohort. Renal function was not influenced by the administered drug combinations, even in patients with pre-existing renal impairment.

KIDNEY

P06 IMPACT OF IMMUNOSUPPRESSIVE DRUGS ON THE BK-POLYOMAVIRUS NON CODING CONTROL REGION (NCCR) ACTIVITY

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Introduction and Background: Reactivation of the BK-Polyomavirus (BKPyV) can cause a polyomavirus associated nephropathy (PyVAN) in approx. 10% of kidney transplant recipients. PyVAN can lead to a gradual functional deterioration and transplant failure. Currently, no direct antiviral therapy to treat BKPyV reactivation is available. It has been shown that mTOR inhibitors can limit BKPyV replication, however the mechanisms underlying this limitation still remains elusive. In this study we aimed to analyze whether the viral promoter which is located in the Non Coding Control Region (NCCR) is affected by mTOR inhibitors.
Methods: We isolated DNA from sera obtained from patients after renal transplantation and amplified full length NCCRs. The amplicons were cloned into a plasmid encoding tdTomato resulting in a reporter system that allows the quantification of NCCR driven early gene expression. To examine the effect of mTOR inhibition on NCCR activity HEK293T cells were transfected with the reporter plasmid and treated with different concentrations of mTORinhibitors and one calcineurin inhibitor. Everolimus (EVE) were used to examine the mTOR1 complex. INK128 were used to examine the dual mTOR1 and 2 complex inhibition. In addition the effect of the calcineurin-inhibitor Tacrolimus on the NCCR activity was examined. 72 h after transfection readout was performed using FACS analysis.
Results and Conclusions: mTOR complex 1 inhibition (EVE) did not reduce early promoter activity. The calcineurin inhibition did not reduce the early promoter activity in relevant concentrations. Treatment with the dual mTOR complex 1 and 2 inhibitor INK128 resulted in a strong inhibition of the early BKPyV NCCR activity.

These data indicate that the impact of EVE on the NCCR activity seems not to be the only underlining effect of the previously published EVE based inhibition of BKPyV replication. Based on the negative impact on the BKPyV NCCR activity INK128 may have an inhibitory effect on the BKPyV replication.

P07 SERUM URIC ACID AND ARTERIAL FUNCTION AFTER RENAL TRANSPLANTATION

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Introduction and Background: Hyperuricemia is associated with an increased risk of cardiovascular disease and chronic allograft nephropathy after renal transplantation. It has recently been demonstrated that treatment of asymptomatic hyperuricemia goes along with an improvement of patient and graft survival. The underlying mechanisms remain elusive. The present study investigates the association of serum uric acid (SUA) and systemic arterial function after renal transplantation.
Methods: In a cross-sectional study arterial function was analyzed in 54 renal transplant recipients by means of pulse wave analysis. Different measurement techniques were combined providing data on pulse wave velocity, augmentation index, small and large artery elasticity, and total peripheral vascular resistance.
Results and Conclusions: The prevalence of hyperuricemia was 87.0%. 33.3% renal transplant recipients received SUA lowering medication. The median SUA concentration was 7.4 mg/dl. There was no significant difference in all of the above mentioned parameters in patients with a SUA <7.4 vs. >7.4 mg/dl ($p > 0.05$ each) and in hyperuricemic subjects with vs. without SUA lowering medication. Linear regression analysis between SUA and both pulse wave velocity and augmentation index showed no significant association ($p > 0.05$ each). This finding remained consistent after adjustment of data for age, time on dialysis, time since transplantation, and systolic blood (partial correlation analysis, $p > 0.05$).

Neither the concentration of SUA nor the pharmacological treatment of hyperuricemia had measurable effects on arterial stiffness. Thus, the beneficial effects of SUA lowering treatment on patient and graft survival cannot be explained by direct effects on arterial function in the present population.

P09 DECEASED DONOR URINARY BIOMARKER SIGNATURE AND THE EFFECTIVENESS OF PERTRANSPLANT LYMPHOCYTE DEPLETION ON EARLY RENAL ALLOGRAFT FUNCTION

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Introduction and Background: Delayed graft function (DGF) associates with increased allograft immunogenicity and decreased long-term survival. We hypothesized that high levels of pre-transplant urinary biomarkers for injury and inflammation amplifies inflammation after reperfusion and Thymoglobulin (Thym) reduces reperfusion injury and DGF.
Methods: We collected urine samples from deceased donors before organ harvest and assessed post-transplant outcomes of these kidneys. Deceased kidney donors and their corresponding 572 kidney recipients were analysed. Urinary injury and inflammatory biomarkers (IL-18, KIM-1, MCP-1, NGAL, C3a, C5a) were analysed.
Results and Conclusions: 90% of the recipients received Thym at a median dose of 5.8 mg/kg. Thym dose was associated with DCD donor status, longer cold ischaemia time, high cPRA. Thym dose did not associate with recipient DGF or posttransplant renal function on day 7 and 12-months and graft failure rate at 1 year. Thym dose did not associate with reduced DGF rate in organs with deceased donor acute injury (defined by AKIN criteria). We found a significant interaction between the 2nd tertile of urinary C5a (and a trend for the 3rd tertile) and Thym dose with the outcome of DGF. The odds of DGF was higher for individuals with an lower Thym dose and elevated C5a (second tertile) (OR (95%CI) 2.36 (1.19,4.68; $p = 0.03$) compared to those with a lower C3a (first tertile). In contrast, individuals with a higher dose of Thym did not have a significantly different association with DGF based on the level of C5a.

These data suggest that high levels of the urinary inflammatory biomarker c5a before transplantation amplifies the recipient inflammatory responses after reperfusion and higher doses of Thymo reduce the rate of recipient DGF in this subgroup.

P10 PRE-TRANSPLANT VERSUS EARLY OR LATE POST-TRANSPLANT PARATHYROIDECTOMY IN SHPT KIDNEY TRANSPLANT CANDIDATES

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Introduction and Background: The timing of parathyroidectomy (PT) in kidney transplant candidates suffering from secondary hyperparathyroidism prior versus early or late after transplantation is still controversial.
Methods: The short-term follow-up cohort comprised 66 patients (52 pre-transplant PT patients, 14 post-transplant PT patients) with one year post-transplant follow-up while the long-term follow-up cohort contained 123 patients (67 pre-transplant PT patients, 56 post-transplant PT patients). Propensity scores (PS) for PT prior versus after transplantation were determined. Risk-adjusted identification of independent risk factors for compromised renal graft function (KDIGO-stage ≥IV) was performed adjusted for PS logits in

multivariable regression analysis. Intra-individual matched-pair analyses were used to identify significant effects of post-transplant PT on graft function as assessed with estimated glomerular filtration rate (eGFR) and paired t-tests.
Results and Conclusion: Donor kidney function KDIGO-stage III ($p = 0.030$; OR=5.191, 95%-CI: 1.100–24.508), donor blood group 0 ($p = 0.005$; OR=0.176, 95%-CI: 0.048–0.642) and post-transplant PT ($p = 0.032$; OR=17.849, 95%-CI: 1.086–293.268) were revealed as independent significant risk factors for compromised renal graft function in the short-term follow-up cohort using PS risk-adjustment. Post-transplant PT had no independent significant influence with PS risk-adjustment in the long-term follow-up cohort ($p = 0.651$). PT after transplantation significantly compromised graft function early after PT and at last follow-up in all post-transplant PT cases ($p \leq 0.004$). PT within the first post-transplant year was associated with significantly compromised graft function until last follow-up ($p = 0.004$) while later post-transplant PT was not ($p > 0.050$).

PT should be conducted prior to transplantation and if not possible preferably after the first post-transplant year.

P11 EXPRESSION OF PD-L1 IN SQUAMOUS CARCINOMA OF THE SKIN OF RENAL TRANSPLANT RECIPIENTS

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Introduction and Background: The incidence of de novo malignancies is significantly increased after renal transplantation. However, standardized incidence rates greatly vary between malignancies. Non-melanoma skin cancer represents a frequent problem following transplantation while the underlying pathophysiology for this increase is complex. Recently, co-inhibitory signals such as PD-L1 expressed by tumor cells have been identified as an integral part in tumor biology. PD-L1 expression is also linked to prognosis in melanoma, renal cancer and lung cancer and represents a pharmacological target in these malignancies. However, for non-melanoma skin cancer the relevance of this mechanism is unclear.
Methods: We studied the expression of PD-L1 in samples of resected de novo squamous cell carcinoma in three renal transplant recipients. PD-L1 expression was analyzed with immunohistochemistry.
Results and Conclusions: At the time of tumor resection, patients were 55 years old (range 44–74), 55 months (35–125) months post renal transplantation with an eGFR of 34 ml/min (16–49). Immunosuppressive therapy consisted of tacrolimus (2 patients), cyclosporine A (1 patient), mycophenolate (3 patients), and corticosteroids (3 patients). PD-L1 expression was observed in one patient treated with cyclosporine A. Approximately 5 percent of tumor cells expressed PD-L1. Squamous cell carcinoma of the skin was found to express the co-inhibitory ligand PD-L1 which may represent a mechanism to escape immune surveillance. Tumor progression in selected renal transplant recipients may be modulated by PD-L1 expression.

P12 TCR NGS BASED EVIDENCE FOR DIFFERENTIAL DIAGNOSIS AND PERSONALIZED THERAPY IN BKV NEPHROPATHY

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Introduction and Background: BKV nephropathy (BKVAN) is a serious complication after renal transplantation (RTx) leading to a graft loss in up to 50% of affected patients. The diagnosis is based on assessment of BKV viral load in serum and histological findings in transplant biopsy. The presentation of BKVAN might mimic acute rejection, but the therapeutic approaches are completely contrary. Thus, specific tools for precise differential diagnosis are required for kidney transplant patients with BKV reactivation and unclear graft function deterioration.
Methods: Here, we present a case of personalized therapy for renal graft function deterioration based on analysis of transplant infiltrated T-cells in a living-related RTx patient with sustained severe BKV-reactivation (VL >400000 copies/ml) and histological findings of acute rejection BANFF IIa. Due to the known difficulties with differential diagnosis, we applied our new technology identifying specificity of tissue infiltrating T-cells. In details, T-cell receptor (TCR) sequences of the graft infiltrated T-cells were analysed by means of next generation sequencing in T-cells obtained from the graft biopsy. The TCRs of the biopsy were compared to BKV-specific and allograft-specific TCRs in peripheral blood.
Results and Conclusions: We found a strong presence of BKV specific T-cells in the transplant. While 12.95% of infiltrated cells had BKV-specificity, allograft-specificity was almost neglectable (1.22%). The following immunomodulating therapy led to the sustained resolution of BKV reactivation and significant improvement of allograft function (creatinine decrease from 4 mg/dl to 2.7 mg/dl) within 2 months. Thus, the identification of the specificity of tissue infiltrating T-cells by TCR NGS is a valuable technique which enables differential diagnosis and personalized therapy.

P13 LOW PRESSURE MACHINE PERFUSION OF THE KIDNEY: ROLE OF COLLOIDAL SUPPORT

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Introduction and Background: Hypothermic machine perfusion (HMP) of the kidney is classically thought to require colloidal support for prevention of edema development during perfusion. Since novel studies recommend drastic reduction of perfusion pressures upon HMP from 60 mmHg to approximately 30 mmHg, this study re-addresses the rheological need for colloids in kidney perfusion.
Methods: Isolated pig kidneys were subjected to HMP for 20 h in a Lifeport® kidney transporter at a pulsatile pressure of 30/20 mmHg using Custodiol-N solution with (MPdex) or without (MP) addition of 50 g/l dextran 40. Kidneys that were simply cold stored (CS) in Custodiol-N served as controls.
Results and Conclusions: Vascular resistance during HMP did not differ between MPdex and MP, nor did renal vascular flow upon isolated warm reperfusion after preservation. However, renal flow after HMP was significantly improved with regard to the control group.

Likewise, renal clearances of creatinine and urea as well as fractional reabsorption of sodium were significantly enhanced after HMP compared to CS, while no differences were observed between MPdex and MP.

We conclude that colloidal support is not a rheological prerequisite for efficient renal preservation by low pressure HMP.

P14 IMPACT OF SPONTANEOUS DONOR HYPOTHERMIA ON GRAFT OUTCOMES IN SOLID ORGAN TRANSPLANTATION

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Introduction and Background: A previous controlled donor intervention trial found that therapeutic hypothermia reduced delayed graft function (DGF) after kidney transplantation. This study investigates the effects of spontaneous donor hypothermia on initial kidney graft function, and evaluates graft survival including heart and liver transplants in the cohort of the randomized dopamine trial (ClinicalTrials.gov identifier: NCT000115115).
Methods: This retrospective cohort study is nested in the randomized dopamine trial, which included 264 hemodynamically stable brain-dead donors between March 2004 and August 2007.
Results and Conclusions: Hypothermia (core body temperature <36°C) was associated with less DGF after kidney transplantation (OR 0.56, 95%CI 0.34–0.91). The benefit was greater when need for more than a single post-transplant dialysis session was analyzed (OR 0.48, 95%CI 0.28–0.82). Donor dopamine ameliorated dialysis requirement independently from hypothermia in a time-relationship with exposure (OR 0.93; 95%CI 0.87–0.98, per hour). Hypothermia did not alter kidney graft survival (HR 0.83, 95%CI 0.54–1.27), while dopamine treatment was associated with improved long-term outcome (HR 0.95, 95%CI 0.91–0.99 per hour). Stratified analyses of non-renal organs in tertiles of the donor's core body temperature disclosed negative effects on heart allograft survival (HR 1.89, 95%CI 1.09–3.27).

Spontaneous donor hypothermia is associated with less DGF but does not appear to affect long-term outcome of the kidney graft. Our data raise safety concerns against therapeutic hypothermia in multi-organ donors when a thoracic transplantation is considered.

P15 ROBOTIC ASSISTED KIDNEY TRANSPLANTATION - 1ST-YEAR-EXPERIENCE

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Introduction and Background: In 2016, first robotic kidney transplants (RKT) were performed in Germany, primarily in Homburg/Saar and afterward in Halle(Saale). In order to provide minimally invasive surgical techniques to both, living-donors and recipients, establishing RKT as a routine procedure in

transplantation is the main purpose. Experiences at transplant center Halle are presented here.
Methods: Since August 2016, $n = 9$ RKT have been done at our center, three more are scheduled. This is the largest number of RKT in Germany. Collected data are part of ERUS RKT Group Registry.
Results and Conclusions: All transplants were living kidney donations (LKD). Mean recipient age was 48.7 ± 11, donor age 54.3 ± 14 years. 56% of recipients had previous abdominal operations. 3/9 were AB0-incompatible, otherwise immunological low-risk profile. Patient and transplant survival as well as primary function rate is 100%. Mean cut-seam time was 303 ± 24, mean handling time 73 ± 11 min. One case showed postop bleeding from the renal capsule with need for laparoscopic revision, another one developed an asymptomatic lymphocele. Mean hospital stay was 14 ± 3.1 days, mean creatinine at discharge was 139 ± 48 μmol/l. Main advantages are minimized invasiveness, 3D representation with magnification, shake-free handling with nearly unlimited degrees of freedom, as well as cosmetic results with insignificantly longer operating times. Limitations include transperitoneal approach, lack of tactility due to atherosclerotic vessels and a higher logistic effort.

RKT extends options for recipients to minimally invasive techniques. Characteristics allow minimized surgical trauma and, ideally, optimized cosmetic results. However, RKT is not suitable for all recipients. Detailed information on (dis-)advantages remain essential. So far, only done in LKD, RKT also is suitable for routine deceased transplantation depending on logistic conditions.

P17 EARLY CONVERSION TO A CNI-FREE IMMUNOSUPPRESSION WITH SRL AFTER RENAL TX – LONGTERM DATA OF A MULTICENTER TRIAL AND IMPLICATIONS FOR DNDSA

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Introduction and Background: Early conversion to a CNI-free immunosuppression with SRL, MMF and steroids was associated with an improved 1- and 3-year renal function as compared with a CsA-based regimen in the SMART study. Recently, there have been reports on increased occurrence of donor specific antibodies (dnDSA) under mTORis.
Methods: Patients were recruited from the core SMART study to primarily investigate the development of dnDSA in a controlled setting.
Results and Conclusions: 74 patients (53% of the core study population) were included, 39 SRL and 35 CsA (ITT analysis) from 6 centers with an average exposition time of 3.7 years for SRL and 7.0 years for CsA. Blood samples for DSA analysis were collected with a mean of 8.7 years after Tx. No statistically significant difference between the therapeutic arms could be detected with respect to the development of dnDSA. The significant benefit regarding GFR (Nankivell) was still detectable under SRL with 64.37 ml/min/1.73 m2 vs. 53.19 ml/min/1.73 m^2 ($p = 0.044$). Considering the whole SMART population ($n = 140$), patient survival does not differ between groups at 5 years or later on. There was a significant difference in graft failure (11.3% SRL vs. 24.6% CsA, $p = 0.045$ log rank test), resulting from an accumulated graft failure rate occurring after 8 years in the CsA group. Significantly more tumors occurred in the CsA arm (15/69 = 22.1%) compared to the SRL arm (4/71 = 5.8%, $p = 0.012$). Reported AEs reflect the known side effect profile of both IS.

In this longterm followup multicenter trial early conversion to SRL did not result in an increased incidence of dnDSA nor increased risk for the graft or recipient. SRL remained beneficial for the graft function.

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P18 THE CHOICE OF RENAL REPLACEMENT THERAPY (CORETH) PROJECT: PATIENT PARTICIPATION, QUALITY OF LIFE AND ECONOMIC CONSEQUENCES

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Introduction and Background: For end-stage renal disease as a technical substitute of the organ function, treatment is often either done by centre haemodialysis (HD) or by peritoneal dialysis (PD). Although both dialysis procedures are resource consuming, a comprehensive cost finding is still lacking in Germany. The aim of the CORETH project is to compare the direct medical and non-medical as well as the indirect costs between HD and PD.
Methods: From 55 nationwide dialysis centres, a total of 780 patients have been surveyed with standardised questionnaires. Information was collected about services at doctor visits, hospitalisations, medications, medical treatments, rehabilitations, transportations and inabilities to work. To compare patients of the HD and PD with regard to relevant covariates, a propensity score (PS) matching at the individual level with a 1:1 matched ratio was conducted. The PS model is estimated by a logistic regression. The cost analysis from the perspective of the statuary health insurance as well as the social perspective of the HD and PD can examine the effect of other determinants on the costs.
Results and Conclusion: 780 patients received either HD ($n = 529$) or PD ($n = 251$). The cohort differed significantly concerning age, gender, education, employment status, net equivalent household income, comorbidities (Charlson Comorbidity Index) and social support. These differences were balanced after PS matching so that 188 matched pairs of HD- and PD-patients were identified. Because the standardised mean differences were ≤10%, the PS matching has achieved a suitable balance between patients of HD and PD (more results to follow). A PS matching for different patients of HD and PD provide a basis for further cost analysis. For a complete contemplation of the costs between HD and PD, unmatched cases should be also analysed.

P19 PPARGAMMA AS A PUTATIVE STRESS MARKER IN T CELLS FOLLOWING KIDNEY TRANSPLANTATION

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Introduction and Background: The identification of biomarkers is important to allow prognosis of diseases and an appropriate therapeutic regimen. Based on our previous findings, characterizing PPARgamma expression in T cells derived from blood of sepsis patients as a marker of disease progression, we were interested to determine whether PPARgamma expression in T cells is altered in dialysis patients or following kidney transplantation (KTX).
Methods: Blood samples of patients one day before and up to 90 days after KTX were drawn. We determined the leucocyte count and the number of $CD3^+$ T cells per ml blood by FACS analysis. PPARgamma mRNA expression in MACS enriched $CD3^+$ T cells was performed by qPCR.
Results and Conclusions: Under immunosuppressive treatment following KTX, we observed a significant decrease of $CD3^+$ T cells in all patients compared to healthy controls. Subpopulations of $CD3^+$ T cells, i.e. $CD4^+$ and $CD8^+$ T cells, were similarly affected. Interestingly, in transplant patients there were two subgroups; one showed upregulated PPARgamma expression in T cells (> 2000 copies/25 ng RNA), whereas in the second group PPARgamma expression remained low (< 2000 copies/25 ng RNA). Considering comorbidities of the allograft recipients, we observed that PPARgamma mRNA expression was high in patients suffering from an acute or chronic infection. Focusing on the role of dialysis, in T cells derived from patients who had not been dialysed after KTX, PPARgamma expression was low, whereas dialysis treatment increased T cell PPARgamma. Most likely the reduced count of $CD3^+$ cells can be attributed to immunosuppression during anti-thymoglobulin treatment, steroids or calcineurin inhibitors. Acute biopsy-confirmed rejection episodes did not occur in our patients. In conclusion, our preliminary study suggests that PPARgamma mRNA expression may be used as a marker for activation of T cells due to infection(s) or reperfusion injury.

P20 IMPAIRED OUTCOME OF KIDNEY TRANSPLANTS FROM DONORS WITH ACUTE KIDNEY INJURY

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Introduction and Background: Given the gap between patients in need of a renal transplantation (RTx) and organs available, transplantation centers increasingly accept lower quality organs, e.g. from donors with acute kidney injury.
Methods: To determine the outcome of kidney transplants from deceased donors with acute kidney injury (AKI, defined as ≥ AKIN stage 1), all 109 kidney transplant recipients who received a renal allograft from donors with AKI between August 2004 and July 2014 at our center were compared to their respective consecutively transplanted patients receiving kidneys from donors without AKI. Patient and graft survival at 5 years after RTx, frequencies of

delayed graft function (DGF, need for dialysis < 1 week post RTx) and biopsy-proven acute rejections (BPAR) within the first year after RTx as well as estimated glomerular filtration rate (eGFR, CKD-EPI) were assessed.
Results and Conclusions: 5-year patient survival was similar between recipients of kidneys from donors with and without AKI ($p = 0.128$), whereas 5-year death-censored graft survival and overall graft survival were decreased in recipients of AKI kidneys (97.2 % vs. 90.7 %, $p = 0.028$ and 91.6 % vs. 80.4 %, $p = 0.011$, respectively). Recipients of AKI kidneys showed higher frequencies of DGF ($p = 0.0015$) and had a reduced eGFR at 7, 90 and 365 days after RTx ($p = 0.002$, 0.001 and 0.003, respectively). Prevalence of patients who had one or more BPAR episodes within the first year after RTx was similar in both groups ($p = 0.872$).

In our cohort, both short-term and long-term outcome was impaired in patients with kidney allografts from donors with AKI, while other groups report higher rates of DGF in recipients of AKI kidneys, but similar long term outcome. Our data indicates that additional factors impairing long term outcome, e.g. cold ischemia time, should be minimized with particular precaution once kidneys from donors with AKI are considered for transplantation.

P21 DELAYED GRAFT FUNCTION IS ASSOCIATED WITH AN INCREASED RATE OF RENAL ALLOGRAFT REJECTION: A RETROSPECTIVE SINGLE CENTER ANALYSIS

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Introduction and Background: The association of delayed graft function (DGF) and biopsy proven acute rejection (BPAR) of renal allografts is controversial. Borderline rejections (BR) comprise a major portion of biopsy results but the significance of such histologic changes is debated. The present study explores the impact of DGF on BPAR with a special emphasis on discriminating the effects of BR.
Methods: Single center analysis of 417 deceased donor kidney recipients (age>18; transplantation date 1/2008–2/2015). Patients with primary non-function were excluded. DGF was defined as the need for dialysis within the first week after transplantation. Acute rejection was defined according to Banff criteria. Cox proportional hazards models were used to examine the relationship of DGF with BPAR within the first year.
Results and Conclusions: No graft loss was observed during the first year after transplantation. DGF significantly associated with BPAR in the first year, irrespective of whether BR was included (HR 1.63, 95% CI 1.12, 2.39) or excluded (HR 1.67, 95% CI 1.08, 2.62).

DGF is significantly associated with rejection - with or without borderline changes - within the first year.

P22 SGLT2 INHIBITION IN KIDNEY TRANSPLANT RECIPIENTS WITH DIABETES

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Introduction and Background: Sodium-glucose cotransporter 2 (SGLT2) inhibition has been shown to reduce cardiovascular mortality and preserve kidney function in patients with type 2 diabetes. Kidney transplant recipients with diabetes demonstrate increased risk and accelerated progression of micro- and macrovascular complications. However, potential concerns of SGLT2 inhibition include volume depletion and acute kidney injury as well as urinary tract infections. Here we report safe application of SGLT2 inhibitors in an ongoing case series of patients after kidney transplantation.
Methods: Kidney transplant recipients started on empagliflozin for better glucose control were included in the analysis. Patients with a stable allograft function (eGFR ≥45 ml/min/1.73 m²) were eligible for SGLT2 inhibition. Empagliflozin was given as add-on to preexisting antidiabetic treatment with dose reduction of the latter. Patients were asked to ensure adequate hydration and urogenital hygiene.
Results and Conclusions: To date, 4 patients have entered the analysis. Median eGFR at baseline was 75 ml/min/1.73 m² with a median time since transplantation of 8,7 years. Median HbA1c prior to treatment was 7.6%, median fasting plasma glucose 168 mg/dl. During follow-up, kidney allograft function remained stable in all patients. No side effects were reported. Required insulin doses decreased by 27% and HbA1c could be markedly improved. Updated results from the ongoing analysis will be presented.

SGLT2 inhibition is safe in selected kidney transplant recipients with diabetes. Glucose control can be improved despite reduction in concomitant antidiabetic treatment. Whether SGLT2 inhibition is able to reduce cardiovascular mortality and improve allograft survival in these patients has to be addressed in further studies.

P25 FIRST ROBOTIC KIDNEY TRANSPLANTATIONS AFTER ROBOTIC KIDNEY LIVING DONATION IN GERMANY

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Introduction and Background: We present the first four cases of transperitoneal pure robotic assisted Kidney transplantation (RAKT), after robotic assisted organ donation from living-related donors, in Germany. In order to reduce the morbidity of open surgery, a robotic-assisted approach for both, the donor and the recipient for Kidney transplantation has been recently introduced. Robotic surgery has proven to decrease operative trauma accompanied by improving operative results in different urological operations in the lower pelvis and the kidney. According to published literature, robotic surgery allows kidney transplantation under optimal operative conditions while maintaining the safety and functional results of the open approach.
Methods: In two cases robotic assisted living kidney donation was performed for right kidneys, two for left kidneys. Recipients suffered from end-stage renal disease (ESRD) and were on dialysis treatment for 1–13 months until TX.
Results and Conclusions: All RAKTs were successfully performed. Total operative time was 298 min (MEDIAN, range 282–318 min), with 67 min WIT (range: 65–71 min) for intracorporeal positioning, and vascular anastomosis until reperfusion, respectively. The estimated blood loss was in all cases <250 cc. The two kidneys showed additional arteries, which had to be reconstructed back-table. In addition, one of the recipients showed a significant drop in central body temperature (34°C) due to crushed-ice, which was dropped into the peritoneal cavity in order keep the donor-organ cooled down. Postoperatively this recipient showed a delayed graft function, and needed 3 times additional hemodialysis treatment. In the fourth case the recipient developed a HUS and needed additional plasmapheresis, no surgical complications were recorded, the organs started urine production immediately. The donors left hospital after 4–5 days. Advantages of RAKT are related to the quality of the vascular anastomosis, the possible lower complication rate and the shorter recovery.

P26 ASSOCIATION OF SERUM UCID ACID LOWERING THERAPY AND RESISTANCE INDEX AFTER RENAL TRANSPLANTATION

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Introduction and Background: Hyperuricemia is a common problem after renal transplantation. It is associated with an increased risk of cardiovascular events and graft loss. We have previously shown that treatment of asymptomatic hyperuricemia may be associated with a benefit in patient and graft-survival. In the present study, we evaluated whether this phenomenon is associated with intrarenal hemodynamic changes as measured by the resistance index (RI).
Methods: We performed a retrospective analysis of 338 renal transplant recipients over a follow-up period of 120 months. The population was stratified into three groups based on examinations at month 12 after transplantation. Group 1 (normouricemia) had a serum uric acid (SUA) concentration <7 mg/dl and never received SUA lowering therapy during follow-up. Group 2 (hyperuricemia, untreated) had a SUA≥7 mg/dl and never received SUA lowering therapy. Group 3 (hyperuricemia, treated) received SUA lowering therapy within the follow-up period.
Results and Conclusions: In cox regression analysis adjusted for age, eGFR, body mass index and postmortal vs. living donation there was a trend to better survival in Group 3. At 12 and 60 months, linear regression analysis were performed between RI and SUA concentrations showing a significant correlation for this group at month 12. The development of RI within the 10 year follow-up period differed between groups: At month 120, RI was significantly higher in untreated hyperuricemic subjects (0.76 ± 0.06) than in the others groups ($p < 0.05$), although it started at a level even lower than the group of treated hyperuricemia subjects at 12 months (0.70 ± 0.08 vs. 0.73 ± 0.08, $p < 0.05$).

SUA lowering therapy is associated with a lower increase of RI over time and a trend to better survival of renal transplant recipients in this retrospective analysis.

P27 ROLE OF BLOOD AS A PERFUSATE FOR THE EVALUATION OF POSTISCHEMIC RENAL FUNCTION IN THE ISOLATED PIG KIDNEY

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Introduction and Background: *Ex vivo* kidney perfusion has been proven an attractive model to study ischemia-reperfusion and preservation injury. This study investigated the putative role of sanguineous or artificial perfusate on renal perfusion characteristic and kidney function in the isolated perfused kidney.
Methods: Porcine kidneys ($n = 6$ per group) were preserved with cold histidine-tryptophan-ketoglutarate (HTK) solution for 18 h at 4°C. Postischemic kidney function was evaluated by 90 min of isolated reperfusion in an established model, using either diluted autologous blood or modified Krebs-Henseleit buffer.
Results and Conclusions: No differences were seen between blood and bloodless reperfusion with regard to postischemic glomerular function (clearances of creatinine and urea), tubular cell integrity (fractional sodium excretion), urine production or oxygen consumption. However, renal perfusate flow was significantly lower in the blood perfused group. On a molecular level mRNA expression of inflammatory parameters (IL6, TNFα, TLR-4) were equally upregulated in both groups.

It is concluded, that functional evaluation of preservation injury by isolated kidney perfusion could be done with blood as well as with bloodless buffer.

P28 RANDOMISED, OPEN-LABEL, COMPARATIVE PHASE IV STUDY ON THE BIOAVAILABILITY OF CICLOSPORIN PRO (TEVA) VERSUS SANDIMMUN® OPTORAL (NOVARTIS) IN PATIENTS WITH STABLE RENAL TRANSPLANTS

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Introduction and Background: Assessment of the bioavailability of Ciclosporin Pro (Teva) versus Sandimmun® Optoral (Novartis) under fasting versus fed conditions in patients with stable renal transplants
Methods: This was a randomised, open-label, repeated-measurement, comparative phase IV trial. The study was conducted with two sequence groups for nutrition condition (Group A: fasting→fed and Group B: fed→fasting) and two treatment phases (29 days Sandimmun® Optoral → 29 days Ciclosporin Pro), each of which covered both nutrition conditions. It served to compare the influence of a high-fat meal on the pharmacokinetics (PK) of Ciclosporin Pro versus Sandimmun® Optoral in patients with stable renal transplants. A total of 31 patients were randomised.
Results and Conclusions: A lesser reduction of bioavailability due to high-fat nutrition of Ciclosporin Pro compared to Sandimmun® Optoral in patients with stable renal transplants in terms of the difference D of ln-transformed bioavailability measured by the primary variables AUCSS,τ, CSS,max, and CSS,min was not shown: For the pharmacokinetic parameter CSS,max the p-value of the one-sided t-test ($\alpha = 0.025$) was 0.1320 in the FAS ($n = 24$) and 0.1820 in the PP ($n = 21$). The reduction of bioavailability of ciclosporin caused by the ingestion of high-fat food immediately before medication intake appeared on average numerically less pronounced under Ciclosporin Pro than under Sandimmun® Optoral. A nutrition effect was found for both study medications with respect to the parameters AUCSS,τ and CSS,max, but not with respect to CSS,min.

In summary, an effect of high-fat breakfast prior to the morning dose on AUCSS,τ and CSS,max was found for Sandimmun® Optoral and for Ciclosporin Pro. This effect appeared numerically slightly more pronounced for Sandimmun® Optoral than for Ciclosporin Pro.

P30 DRUG-INDUCED CYTOCHROME-P450 INDUCTION AS THERAPY FOR CALCINEURIN INHIBITOR INTOXICATION

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Introduction and Background: Management of calcineurin inhibitor (CNI) therapy in kidney transplant recipients may be complicated due to polypharmacy. As CNI undergo extensive metabolism by cytochrome-P450 enzymes (CYP) drug-induced CYP-inhibition poses risk for elevated CNI blood concentrations. Here, we report on two kidney transplant recipients treated with tacrolimus who presented with signs of tacrolimus intoxication at admission.
Methods: 56 year-old patient A was started on antiviral medication ombitasvir, paritaprevir, ritonavir and dasabuvir for hepatitis-C virus treatment 3 days prior to hospitalization. And 54 year-old patient B was treated with clarithromycin for pneumonia.
Results and Conclusions: Both therapies cause drug-induced CYP-inhibition and both patients displayed highly elevated tacrolimus trough serum concentrations (C0) (tacrolimus C0 max [ng/ml]: pt. A 67.8, pt. B 46.0) and acute kidney injury (creatinine max [mg/dl]: pt. A 4.0, pt. B 4.3). After application of CYP-inducing agents rifampicin (600 mg, 1–2x per day for 3 days) and phenytoin (200 mg, 2x per day for 4 days) respectively, tacrolimus levels were reduced within 4 to 5 days (tacrolimus C0 at discharge [ng/ml]: pt. A 4.0, pt. B 4.3) and renal function recovered (creatinine at discharge [mg/dl]: pt. A 2.1, pt. B 2.3). Treating severe CNI-intoxication is an infrequent yet emergent condition. These results add to the knowledge of therapeutic drug-induced CYP-induction.

P31 INFLUENCE OF RENAL TRANSPLANTATION ON PROSTATE CANCER PATIENTS SURVIVAL

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Introduction and Background: Questioning the effects of a renal transplantation and previous insufficiency on the outcome of patients with prostate-cancer, we retrospectively looked at 55 men who were treated between 27th of April 1988 and 31st of December 2016 in the NTZ Halle.
Methods: Based on the course of disease we formed two groups. The patients in Group I ($n = 38$) first had a renal transplantation and subsequently developed prostate cancer. Group II ($n = 17$) includes patients who got a renal transplant after being diagnosed with prostate cancer. The patients were between 40 and 74 years old at the time of the cancer diagnosis (mean age 62.5 ± 7.4 years) and the 1-, 3- and 5-year survival rates were analysed.
Results and Conclusions: The patients of group I, who developed prostate cancer under immunosuppression after renal transplantation have a lower 1-, 3- and 5-year survival rate than people at the same age from general population without such a pre-existing illness. The risk of death in group I five years after being diagnosed with prostate cancer is 4,6 times as high as in the general population. The patients of group II, who were treated with a renal transplantation after the diagnosis prostate cancer also have a lower 1-, 3- and 5-year survival rate than people at the same age from general population. So the risk of group II to be dead five years after the cancer diagnosis is 3, 4 times as high as in the same aged general population.

In summary, the risk of being dead five years after prostate cancer diagnosis is in both groups higher compared to the healthy general population. The immunosuppression might have a negative effect on the outcome of the patients. In the same way, you can assume that a failure of renal function reduces the survival time.

P32 PATIENT AND GRAFT SURVIVAL IN PATIENTS WITH PREVIOUS MALIGNANCIES AFTER CONVERSION MTOR INHIBITOR SIROLIMUS IN A LARGE GERMAN COHORT

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Introduction and Background: Renal transplant recipients have an increased cancer risk. The mTOR inhibitor sirolimus has immunosuppressive and antitumor effects.
Methods: In this retrospective study 10 German transplant centers set up a database of 726 patients who were switched to sirolimus consisting immunosuppression. We show data of patients with a malignancy prior to conversion and a survival analysis comparing the tumor entities.
Results and Conclusions: In 214/726 patients a tumor entity was known. Most common entity were skin cancers ($n = 137$) and solid cancers ($n = 102$). Lymphoma ($n = 15$) and hematological tumors ($n = 3$) were less frequent. In skin cancers, basalioma (43.1%) and squamous cell carcinoma (35.0%) were most frequent. Patients with skin tumors were predominantly male, younger at transplantation and having a longer ischemia time compared to other non-skin-related tumors. The initial immunosuppression consisted less frequently of IL-2-receptor antibodies or mycophenolate but more often of azathioprine. At the time of conversion to sirolimus patients were older, longer transplanted, had less severe proteinuria. In solid cancers renal cell carcinoma (30.4%) was most reported followed by colon and breast cancer (both 12.7%). Patients with solid cancer had more frequently an initial immunosuppression with cytotoxic antibodies and mycophenolic acid and less frequently with azathioprine as compared to patients without a solid tumor. At the time of conversion to sirolimus patients were shorter transplanted and had a higher maintenance dose at 3 months post conversion. The 5-year-patient-and-graft-survival according to the entity was significantly ($p < 0.001$) better in patients with a

skin tumor than with a solid or other tumor combination. Patients with previous malignancies may benefit from conversion to sirolimus.

P34 MAINTENANCE IMMUNOSUPPRESSIVE THERAPY WITH BELATACEPT AFTER HEART AND KIDNEY TRANSPLANTATION

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Belatacept (BELA) is a selective T-cell costimulation blocker indicated for prophylaxis of organ rejection kidney transplant recipients approved in 2011. Currently, however, there is only limited published information on the use of BELA in heart transplant recipients.

In 2012 a 46-year old male man received a heart transplantation due to valvular cardiomyopathy end stage heart failure. His first lane immunosuppressive therapy after heart transplantation was Cyclosporine A, MMF and steroids. Due to multiple complications before and after heart transplantation the patient developed severe renal insufficiency which rapidly progressed to end stage renal disease although immunosuppressive therapy was switched from MMF to the mTOR-inhibitor Everolimus (EVR). Starting in January 2013 the patient was on regular dialysis until March 2014 when a living related kidney transplantation was preformed from his 76-years old mother. Renal transplant function was excellent with creatinine levels of 1.5 mg/dl from April 2014 until March 2016 when eGFR declined and creatinine increased to 2.6 mg/dl. Immunosuppressive therapy was changed from Cyclosporine A and EVR to BELA and EVR assuming that kidney transplant function was reduced due to cyclosporine-nephrotoxicity. BELA is given at a dose of 5 mg/kg bw once monthly and EVR trough levels are between 5–8 ng/ml. Kidney function improved to creatinine levels ranging from 1.9–2.1 mg/dl. Function of the heart allograft was excellent during the 9 months follow up period after switch to BELA.

This case demonstrates that BELA can be considered as maintenance immunosuppressive therapy in combination with EVR in patients after heart and kidney transplantation and might be a new and promising opportunity to treat patients after heart transplantation with reduced renal function to spare kidney function. However, long-term use and outcomes in larger heart transplant populations are needed.

P35 FAILURE OF ECULIZUMAB TREATMENT FOR THROMBOTIC MICROANGIOPATHY (TMA) ASSOCIATED WITH ACUTE HUMORAL REJECTION IN A RENAL TRANSPLANT RECIPIENT

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The atypical hemolytic uremic syndrome (aHUS) is a rare cause of end-stage renal disease but is described to recur in 6% up to 71% of renal transplant recipients within the first posttransplant year. Neither the frequency nor the optimal treatment modality of secondary TMA associated with acute rejection is well characterized.

We report on a 59 year old patient with ADPKD who received a preemptive live-donor renal transplant from his sister. After an uneventful posttransplant course with good graft function, the patient experienced a biopsy-proven acute antibody-mediated interstitial rejection on day 40. As treatment (steroid pulses, rabbit ATG and immunoabsorption / IVIG) showed no response, eculizumab was initiated when TMA was detected together with ongoing transplant glomerulitis (without any interstitial rejection) in the repeat biopsy. Despite complete inhibition of both the classical and alternative complement pathways graft function showed no improvement and a final biopsy detected interstitial fibrosis and tubular atrophy of the cortex (65% concerned; no TMA or rejection). We found no donor-specific antibodies (DSA), neither against HLA (IgG, IgM) nor against non-HLA antigens (MICA, antiphospholipid antibodies, angiotensin II- and endothelin-receptor antibodies, anti-Fga antibodies). Furthermore, T- and B-cell crossmatches were negative, as were the ELISA and anti-endothelial cell crossmatches. Genetic testing found no mutation of the investigated genes for aHUS.

Our report describes an uncommon case of secondary TMA associated with acute humoral rejection, without detection of any DSA. Even eculizumab rescue for TMA associated with ongoing humoral rejection as detected in the repeat biopsy was unsuccessful despite effective complement inhibition. Whether an earlier eculizumab initiation would have prevented TMA and graft failure, is a point of discussion.

P36 RADICAL PROSTATECTOMY IN RENAL-TRANSPLANTED PATIENTS

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Introduction and Background: Our target was to find out the effects of a radical prostatectomy in prostate cancer patients with a kidney transplant. To examine the renal function we surveyed the glomerular filtration rate (GFR) - as one important marker - of 20 patients who were treated in the NTZ Halle between the 27th of April 1988 and the 31st of December 2016. Patients were only included into our study if a minimum of one pre- and five post-operative GFR values had been documented.
Methods: One day before the radical prostatectomy took place, the GFR averaged out at 42 $\pm$ 16 ml/min. Based on this we classified our sample in stages of renal failure: no patient in stage I, two in stage II, twelve in stage III, six in stage IV and no one in stage V.
Results and Conclusions: In most patients the GFR increased directly post-operative. During the following two months this value recovered in the majority, only three patients had to be allocated to a worse stage than before. In two of these three a chronic renal failure with a GFR lower than 15 ml/min was diagnosed. Thirteen were still in the same stage as before, even a bettering was detected in four patients.

We can guess that a radical prostatectomy has various effects on the renal transplant function in our sample, including total renal failure as well as normal GFR values. In summary not only the radical prostatectomy but many different individual aspects affect the kidney transplant function.

LIVER

P37 COST AND RISK FACTOR ANALYSIS FOR PARTICIPATION IN REHABILITATION PROGRAMS AFTER LIVER TRANSPLANTATION

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

Participation in RPs is associated with prolonged graft and patient survival. Patients without complications more often participate in RP, especially without the burden of a chronic underlying disease, while patients with post-transplant complications would be expected to benefit more. The higher expenses in the period 1–3 years after transplantation in the RP-group are well explained by overall shorter survival in the non-RP group.

P38 LINEAR GROWTH AND SEXUAL MATURATION WITH EVEROLIMUS PLUS REDUCED CALCINEURIN INHIBITOR-BASED REGIMEN IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS: 12-MONTH RESULTS FROM CRAD001H2305-STUDY (NCT01598987)

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Introduction and Background: Post-Tx immunosuppression (IS) may affect linear growth and pubertal development of pediatric liver transplant recipients (pLTxR). H2305 evaluated efficacy and safety of everolimus (EVR)+reduced tacrolimus (rTAC) or cyclosporine A (rCsA). We present 12M linear growth and sexual maturation results from H2305.
Methods: This 24M, multicenter, open-label, single-arm, prospective study included pLTxR treated with CsA/TAC±mycophenolate±steroids within M1 to M6 post-Tx. Eligible patients received EVR (trough level 3–8 ng/ml)+rTAC or rCsA±steroids from baseline (BL) up to M24. Linear growth was assessed by height weight and body mass index (BMI). Sexual maturation was assessed by ranges of gonadal axis hormones and Tanner staging [TS] in age groups <8 and ≥8 year. Based on data monitoring committee recommendation recruitment was prematurely stopped. Patients <7 year were reverted to standard-of-care IS.
Results and Conclusions: 50 of 56 patients were available for M12 evaluation. From BL to M12 patients had no change(44%) or increase(42%) in height and no change(24%) or increase(48%) in weight. Most patients had normal ranges of thyroid-stimulating hormone(97.5%), T4(100%) and inhibin B (95.5%) levels at M12. Almost 60% had free T3 levels above normal range. 87.5% males had testosterone levels below normal range. Patients <8y belonged to TS 1 or 2, whereas 3/5 males and 3/4 females ≥8y had achieved TS 3–5 by M12. No events of abnormal sexual maturation were reported during study period.

Although limited by sample size, the study findings indicate that EVR with rTAC or rCsA does not appear to negatively impact linear growth or sexual maturation in pLTxR up to 12M post-initiation. Follow-up beyond 12M is required to define the effect of low testosterone levels.

P40 PRETRANSPLANT CORONARY ARTERY DISEASE IS THE STRONGEST PREDICTOR FOR MYOCARDIAL INFARCTION AND CARDIAC DEATH AFTER LIVER TRANSPLANTATION

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Introduction and Background: Cardiovascular disease is a serious problem of liver transplant (LT) recipients because of increased cardiovascular risk due to immunosuppressive therapy, higher age, intraoperative risk and comorbidities (such as diabetes and nicotine abuse). Our aim was

- to evaluate frequency of the cardiovascular endpoints myocardial infarction and/or cardiac death (CVE) after LT
- to investigate correlations of CVE post LT with pretransplant patient characteristics.

Methods: In total, data from 352 LT patients from our center were analyzed. Patients were identified from an administrative transplant database, and all data were retrieved from patients" charts and reports.
Results and Conclusions: During the mean follow-up of 4.2 (±3.1) years, 10 cases of CVE were documented (six myocardial infarctions and four coronary deaths). CVE did not correlate with classic cardiovascular risk factors such as body mass index ($p = 0.089$), total cholesterol ($p = 0.458$), hypertension ($p = 0.747$), smoking ($p = 1.0$) and pretransplant diabetes mellitus ($p = 0.146$). The only patient characteristic correlated to CVE was pretransplant coronary heart disease (CHD) ($p = 0.024$), that was found in 24 patients (6.8 %).

Overall the frequency of CVE in LT recipients is low in our observation period (6.8 %). CVE was correlated to CHD ($p = 0.024$), but even in patients with CHD the frequency of CVE was not very high (12.5 %). Therefore, stable coronary heart disease should be no absolute contraindication for LT, but these patients should be monitored carefully after LT.

P41 A NOVEL SURGICAL MODEL AS A FOUNDATION FOR FURTHER LIVING ORGAN ENGINEERING *IN VIVO*

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Introduction and Background: Partial organ decellularization *in-vivo*, also called chemical resection, was first described by Pan (IntJBiochem&CellBiol 2016) as a potential treatment option instead of surgical resection. They achieved selective perfusion of the right inferior liver lobe in rats at the expense of completely blocking portal vein and inferior cava.

Our study aims for establishing a novel method for partial liver perfusion in-vivo with preservation of physiological blood flow to the remaining liver. In the long run, we aim to conduct organ engineering *in-vivo* and to explore repopulation and functional recovery of the decellularized liver lobe.
Methods: Using male Lewis Rats ($n = 6$), we created a by-pass circulation within left lateral (LL) lobe. The left portal vein was blocked distally using 6-0 silk suture and cannulated (24G basket catheter), whereas the LL hepatic vein was cannulated (22G basket catheter) and blocked distally with a micro-clamp.
Results and Conclusions: Using heparinized saline, the targeted liver lobe was indeed perfused selectively from the inlet and drained via the outlet we designed. Physiological perfusion of the other liver lobes was maintained as well as blood flow through the vena cava.

Selective perfusion of the targeted liver lobe while preserving the blood flow of vena cava and the remaining partial liver is technically feasible in rats. Our novel method of partial liver perfusion may provide the foundation for further exploring liver engineering (hepatic cells or stem cells transplantation) and the process of liver functional recovery *in-vivo*.

P42 PROGNOSTIC FACTORS FOR LONG-TERM SURVIVAL ≥15 YEARS AFTER PRIMARY PEDIATRIC LIVER TRANSPLANTATION AFTER POST-MORTAL ORGAN DONATION

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Introduction and Background: Factors that determine long-term survival ≥15 years after transplantation independent of short-term mortality are still unknown but are required to optimize the utility of transplantation.
Methods: 148 patients with survival after pediatric primary liver transplantation ≥15 years or death between the second and fifth post-transplant year were analyzed. Multivariable logistic regression model were used to identify independent prognostic factors.
Results and Conclusions: Prognostic factors for long-term survival ≥15 years were donor BMI ($p = 0.007$; OR=0.827, 95%-CI=0.751–0.970), the number of surgical complications ($p = 0.019$; OR=0.358, 95%-CI=0.162–0.805), the donor cause of death cerebrovascular accident ($p = 0.047$; OR=5.910, 95%-CI=1.004–34.784) and the donor cause of death cranial injury ($p = 0.024$; OR=5.662, 95%-CI=1.294–24.779).

A higher donor BMI and post-operative surgical complications decrease the likelihood of long-term survival while the donor causes of death cerebrovascular accident and cranial injury increase the likelihood of long-term survival. This result implies that post mortem donors with high BMI should be avoided for pediatric liver transplantation to increase long-term utility of liver transplantation in children especially in those cases with donor causes of death other than cerebrovascular accident or cranial injury.

P43 RECIPIENT CELIAC TRUNK STENOSIS IS A SIGNIFICANT RISK FACTOR FOR EARLY HEPATIC ARTERY THROMBOSIS AFTER LIVER TRANSPLANTATION

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Introduction and Background: Hepatic artery thrombosis (HAT) is a rare but severe complication after liver transplantation (LT). The aim was to study risk factors of HAT, notably a recipient celiac trunk stenosis and a variant anatomy of the recipient hepatic artery, in our single center experience.
Methods: Between 1997 and 2013, a total of 709 LT in 618 patients were performed at our center and collected in a prospective SPSS database. Early (<30 days) HAT (EHAT) occurred in 18, late HAT (LHAT) in 12 patients. Patients with EHAT and LHAT were compared to a randomized control group of 100 patients without HAT. Recipient celiac trunk stenosis was assessed on pre-LT imaging by two independent radiologists. Univariate analysis by Fishers exact test and a multivariate logistic regression were used the EHAT group, a descriptive analysis in the LHAT group.
Results and Conclusions: In univariate analysis, stenosis of the recipient celiac trunk, presence of accessory hepatic arteries, retransplantation, use of an aortic conduit and the amount of transfused FFP were significantly associated with the development of EHAT. Upon multivariate regression, only a stenosis of the celiac trunk ($p = 0.001$) and retransplantation ($p = 0.002$) were significantly associated with EHAT. LHAT seemed to be associated with the use of an aortic conduit and retransplantation.

This is the first study to identify a stenosis of the recipient celiac trunk as a significant risk factor for the development of early hepatic artery thrombosis after LT. Patients should be systematically screened. LHAT seemed to be associated with the use of an aortic conduit and retransplantation.

P44 LIVER TRANSPLANTATION AND LIVER RESECTION FOR CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA: COMPARISON OF LONG-TERM SURVIVALS

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Introduction and Background: Both liver transplantation (LT) and liver resection (LR) represent curative treatment options for hepatocellular carcinoma (HCC) in patients with liver cirrhosis. In this study, we have compared outcomes between historical and more recent patient cohorts scheduled either for LT or LR, respectively.
Methods: Clinicopathological data of all patients with HCC and cirrhosis who underwent LT or LR between 1989 and 2011 were evaluated. Overall survival of patients with HCC within the Milan criteria (MC) was analyzed focusing on changes between different time periods.
Results and Conclusions: In total, 364 and 141 patients underwent LT and LR for HCC in cirrhosis, respectively. Among patients with HCC within MC, 214 and 59 underwent LT and LR, respectively. Postoperative morbidity (37% vs. 11%, $p < 0.0001$), but not mortality (3% vs. 1%, $p = 0.165$), was higher after LR than after LT for HCC within MC. In the period 1989–2004, overall survival (OS) was significantly higher in patients who underwent LT compared to LR for HCC within MC (5-year OS: 77% vs. 36%, $p < 0.0001$). Interestingly, in the more recent period 2005–2011, OS was comparable between LT and LR for HCC within MC (5-year OS: 73% vs. 61%, $p = 0.07$).

We have noted improved outcomes after partial hepatectomy in recent years, comparable to stable results after LT for cirrhotic patients with HCC. Whether those improvements are due to advances in liver surgery such as laparoscopic approaches and improved perioperative therapy of patients with cirrhosis, appears plausible. In the light of organ shortage, patients with HCC and compensated cirrhosis should be evaluated for liver resection in specialized hepatobiliary centers.

P45 BILE DUCT DAMAGE AFTER STORAGE OF DECEASED AND LIVING DONOR LIVERS IN LIVER TRANSPLANTATION

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Introduction and Background: Biliary lesions belong to a group of disorders constituting major complications in patients undergoing orthotopic liver transplantation (OLT). It is suspected that vascular damage of the donor bile duct might play a major role in the pathogenesis of postoperative biliary complications.
Methods: We took a sample of the donor bile duct for histological evaluation during OLT prior to recirculation of the hepatic artery and prior to biliary anastomosis. Organ retrieval was performed according to the protocol of the Deutsche Stiftung für Organtransplantation. Aortic flush perfusion was performed used histidine–tryptophan– ketoglutarate (HTK) solution. After retrieval, the cystic duct was ligated and the bile ducts were rinsed with HTK solution. We evaluated mucosal loss ≥50%, intramural bleeding ≥50%, thrombi, vascular lesions, and arteriolonecrosis. Lesions were correlated with donor age, ischemia time and type of transplantation (living donor liver transplantation vs. deceased donor liver transplantation). Statistical evaluation was performed by chi-square analysis.
Results and Conclusions: Between 2013 and 2017, 56 consecutive biopsies were available for evaluation, 41 biopsies of deceased donors and 15 biopsies of living donors. The median donor age was 55 (14–80) years. Mucosal loss ≥50%, intramural bleeding ≥50%, thrombi, vascular lesions, and arteriolonecrosis were observed in 4%, 18%, 45%, 20%, 15%, and 39%, respectively. Only one specimen showed no lesions. One, two, three, four and five different lesions were seen in 23%, 29%, 21%, 18%, and 7%, respectively. Neither number nor kind of lesion was statistically significantly correlated with the donor age, ischemia time or the type of transplantation.

Vascular damage of the donor bile duct occurs very frequently during liver transplantation. Donor age and type of type of transplantation seem to have no influence on the type of bile duct damage.

P46 MAJOR EXTENDED DONOR CRITERIA PREDICT OUTCOME AFTER LIVER TRANSPLANTATION

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Introduction and Background: This study aimed to identify most relevant, major EDC (mEDC) predictive of post-liver transplantation (LT) outcome in the MELD-score era.
Methods: We included 465 consecutive LTs in a single-center setting and examined the EDC: donor age >65 years, BMI >30, malignancy, drug abuse history, ICU-stay/mechanical ventilation >7 days, aminotransferases >3x normal, serum bilirubin >3 mg/dl, serum-Na+ >165 mmol/l, positive hepatitis serology, biopsy proven macrovesicular steatosis (BPS) >40%, and cold ischemia time (CIT) >14 h. Primary- and delayed non-function (PNF and DNF), short- (90-day), mid- (1-year) and long-term (5-year) graft survival were of primary interest.
Results and Conclusions: We observed no significant differences in graft and patient survival between the organ recipients with ≥1 EDC and no EDC. Multivariate analysis identified BPS of >40% (HR 10.5 95% CI 3.6–30.3, $p < 0.001$), donor age of >65 years (HR 2.0 95% CI 1.1–3.4, $p = 0.017$), and CIT of >14 h (HR 2.0 95% CI 1.1–3.8, $p = 0.025$) as major EDC (mEDC) that predicted post-LT graft failure. Concomitant presence of mEDC increased the graft failure rates at any investigated time-point compared with cases without these parameters (PNF 2.4 vs. 11.4%; 90-day 3.3 vs. 17.1%; 1-year 7.5 vs. 25.7%; 5-year 7.5 vs. 28.6%, all $p < 0.05$). Five-year graft survival and patient survival were significantly lower in recipients of organs with ≥1 mEDC compared with others ($p = 0.005$ and 0.014). In conclusion, donor age of >65 years, BPS of >40% and CIT of >14 h are the most relevant EDC that decrease long-term patient-, and short- and long-term graft survival. These parameters downgrade the significance of the rest, minor EDC. Organ allocation algorithms based on mEDC should be therefore put into focus and evaluated.

P47 PROGNOSTIC FACTORS FOR LONG-TERM SURVIVAL ≥15 YEARS AFTER PRIMARY ADULT LIVER TRANSPLANTATION

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Introduction and Background: Factors that determine long-term survival ≥15 years after transplantation independent of short-term mortality are still unknown but are required to optimize the utility of transplantation.

Methods: 543 patients with survival after adult primary liver transplantation >15 years or death between the second and fifth post-transplant year were analyzed. Multivariable logistic regression models were used to identify independent prognostic factors.
Results and Conclusions: Prognostic recipient factors for long-term survival ≥15 years were age >44–≤54 years (p = 0.006; OR = 0.444, 95%-CI = 0.248–0.795), age >54 years (p < 0.001; OR = 0.211, 95%-CI = 0.117–0.379), acute liver failure (p = 0.023; OR = 2.495, 95%-CI = 1.063–5.855), alcoholic cirrhosis (p = 0.007; OR = 0.311, 95%-CI = 0.131–0.739), hepatocellular carcinoma (p < 0.001; OR = 0.235, 95%-CI = 0.135–0.411) and primary biliary cirrhosis (p < 0.001; OR = 5.405, 95%-CI = 2.016–14.493).

Prognostic donor factors for long-term survival ≥ 15 years were age >48 years (p = 0.005; OR = 0.372, 95%-CI = 0.186–0.743), donor BMI >23.9–≤26.0 (p = 0.040; OR = 0.514, 95%-CI = 0.272–0.971), donor BMI >26.0 (p = 0.005; OR = 0.382, 95%-CI = 0.195–0.759), donor causes of death cerebrovascular accident (p < 0.001; OR = 3.345, 95%-CI = 1.887–5.932) and cranial injury (p < 0.001; OR = 3.810, 95%-CI = 2.067–7.023).

Durations of surgery >5.3–≤6.7 h (p = 0.019; OR = 2.074, 95%-CI = 1.130–3.807), >6.7 h (p = 0.005; OR = 2.583, 95%-CI = 1.329–5.018), the number of surgical complications (p = 0.011; OR = 0.597, 95%-CI = 0.401–0.890) and biliary leaks (p = 0.018, OR = 0.292, 95%-CI = 0.106–0.629) were also relevant.

Recipients with alcoholic cirrhosis or hepatocellular carcinoma should not receive organs from older donors with higher BMIs as all of these factors decrease the likelihood of long-term survival. Faster transplant operations should be avoided as they decrease the likelihood of long-term survival.

P48 IMPACT OF CALCINEURIN INHIBITOR THERAPY ON BRAIN-DERIVED CYTOKINES AFTER LIVER TRANSPLANTATION

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Introduction and Background: Calcineurin inhibitors (CNI) may induce long-term neurotoxicity in patients after liver transplantation (LT). Alteration of the cerebral immune system resulting in neurodegeneration is discussed as possible mechanism. Our study aimed to measure the impact of CNI therapy on plasma levels of brain- and T-cell derived cytokines.
Methods: The plasma levels of cytokines linked with T-cell activation (e.g. IFN-γ) and brain derived cytokines (brain derived neurotrophic factor (BDNF), soluble neural cell adhesion molecule (sNCAM) and platelet derived growth factor (PDGF-AA and PDGF-AB-BB) were measured by immunoassay in blood samples from 82 patients about 10 years after LT (17 CNI free, 35 CNI low dose and 30 standard dose CNI immunosuppression). Additionally, psychometric testing and cerebral magnetic resonance imaging was performed to assess cognitive function and structural alterations of the brain. 33 healthy subjects adjusted for age, gender and education served as controls.
Results and Conclusions: IFN-γ levels were significantly higher compared to controls only in the CNI free patients (p = 0.027). BDNF levels were significantly lower in patients treated with CNI (CNI low: p < 0.001; CNI standard: p = 0.016) compared to controls. PDGF-AA and AB-BB levels were significantly lower in the CNI low dose group (p = 0.004) and for PDGF-AB-BB also in the CNI standard dose group (p = 0.029) compared to controls. sNCAM levels did not differ between the groups. BDNF and PDGF-AA were negatively correlated with cognitive function and brain volume (p < 0.05) in the CNI low dose group.

CNI do not only influence signaling pathways in lymphocytes, but seem to play a role in the regulation of the cerebral immune system as well. Our results imply that CNI suppress the neurotrophin BDNF and the growth factor PDGF, both crucial for neuronal signaling, cell survival and synaptic plasticity which may lead to altered behavior and neurodegeneration.

P49 MODELLING THE PROTEIN QUALITY CONTROL OF TRANSTHYRETIN IN HEPATOCYTE-LIKE CELLS

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Introduction and Background: Transthyretin-related hereditary amyloidosis (ATTR) is caused by mutations of transthyretin (TTR), primarily expressed by the liver. A competition between ER-assisted folding (ERAF) and degradation (ERAD) of TTR seems to be an important parameter of the disease. We took advantage of induced pluripotent stem cell-derived (iPSC) hepatocyte-like cells (HLCs) to study whether pathogenic mechanisms of ATTR are linked to the protein quality control (PQC).
Methods: Urine from ATTR patients (n = 5) and healthy individuals (n = 4) was processed for isolation of renal epithelial cells, followed by reprogramming into iPSCs and differentiation towards hepatocytes. The hepatic character of HLCs was assessed by functional analyses, gene expression profiling and immunostainings. qPCR was used to analyse gene expression. Protein expression was determined by western blot and ELISA.
Results and Conclusions: HLCs derived from ATTR patients carrying three different mutations of TTR showed high expression of hepatic markers, especially TTR. 39 genes related to PQC were analysed in HLCs, with 32 genes coding for chaperones predominantly located intracellular and 7 located extracellular. Expression of extracellular chaperones was identified to be differently regulated in ATTR patients. SERPINA1 expression was identified to be differently expressed in ATTR and healthy donor HLCs post-TTR downregulation suggesting a regulated expression of variant forms of TTR. Our data show that HLCs derived from ATTR patients are an excellent model to study patient-specific disease mechanisms in the genuine genetic background. Identification of PQC genes involved in chaperoning of variant TTR, e.g. SERPINA1, might illume amyloidogenic pathways and pave the way to new therapy approaches.

P50 EFFICACY AND SAFETY OF EVEROLIMUS (EVR) WITH REDUCED EXPOSURE TACROLIMUS OR CYCLOSPORINE IN PEDIATRIC LIVER TRANSPLANTATION RECIPIENTS (PLTXR): 24-MONTH RESULTS FROM H2305-STUDY (NCT01598987)

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Introduction and Background: EVR with reduced tacrolimus (rTAC) provides anti-rejection efficacy and preserves renal function (RF) in adult LTx, yet data on EVR use pLTxR are limited. Here we present efficacy, RF and safety of EVR+rTAC/reduced cyclosporine (rCsA) in pLTxR.
Methods: In this 24M, multicenter, open-label, single-arm, prospective study, pLTxR (≥1M and <18y) treated with CsA/TAC±mycophenolate±steroids were enrolled from M1 to M6 post Tx. Primary objective was evaluation of RF (eGFR; Schwartz formula) from EVR start to M12. Based on data monitoring committee recommendation, recruitment was prematurely stopped due to increased risk of PTLD, serious infections in patients <7y.
Results and Conclusions: Of 56 patients, 25 were <2y and 31 were 2- < 18y. Mean age was 4.9y at BL. EVR and CsA (n = 6) or TAC (n = 50) C0 were within target ranges up to M24 for most patients. Mean and median EVR C0 were higher in <2y vs. 2- < 18y patients. Mean TAC C0 was near the upper end of target range up to M6. Same trend was observed for CsA C0 from week 1 to M3. Mean observed eGFR at BL, M12 and M24 was 90.5(22.2), 96.7(17.8) and 92.2(14.9) ml/min/1.73 m², respectively. Mean eGFR increased by 6.2 and 4.5 ml/min/1.73 m² from BL to M12 and M24, respectively. M24 data is based on 36% of patients compared to BL. 2 tBPAR episodes were reported but no graft loss or death. PTLD was reported in 6(10.7%) patients, 3 each in <2y and 2- < 18y (1 case reported 1y post study completion). No negative effect on growth or sexual development was noted.

Despite good RF, the study outcomes suggest overimmunosuppression, as evident by low tBPAR, high rates of PTLD and serious infections. However, evidence is limited due to premature termination of recruitment and high rate of treatment discontinuation.

P51 THE "WEEKEND EFFECT" IN LIVER TRANSPLANTATION - A RETROSPECTIVE SINGLE CENTRE STUDY

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Introduction and Background: The "weekend effect" describes a phenomenon whereby patients admitted to hospitals on weekends are at higher risk of complications, worse outcome and death compared to those admitted

during weekdays. However, it remains unknown if the "weekend effect" applies to liver transplantation (LT).
Methods: We retrospectively analysed data from 326 LT Patients between January 2006 and May 2016 and grouped patients based on time of LT (Saturday, Sunday vs. weekday). We assessed one-year patient and graft survival, biopsy proven acute rejections (AR), primary non-function (PNF), surgical complications requiring re-operation, length of stay and number and length of re-admissions.
Results and Conclusions: We identified 243 patients (74.5%) with an LT performed during the week and 83 (25.5%) receiving LT on the weekend. Potential confounders such as age, gender, indication for LT, cold and warm ischaemia time, MELD score and number of high-urgency LTs were all similar between the two groups. One-year patient survival (74.1% vs. 72.3%, $p = 0.665$) as well as graft survival (71.6% vs. 66.3%, $p = 0.307$) were similar between weekday and weekend LT. Frequencies of AR (14.4% vs. 19.3%, $p = 0.297$) and PNF (7.8% vs. 12.0%, $p = 0.266$) were also not different between weekday and weekend LT. The rate of complications requiring re-operation was 57.6% for weekday and 57.8% for weekend LT ($p = 1$), with re-transplantation frequencies of 9.1% and 10.8% ($p = 0.666$), respectively. The initial hospital stay was marginally longer for weekday patients (39d vs. 30d, $p = 0.051$). In conclusion, the findings suggest that there was no "weekend effect" regarding outcomes after LT at our centre. While the "weekend effect" has been described for various time-sensitive acute conditions and emergencies such as acute myocardial infarction, the absence of the "weekend effect" in LT could be due to highly specialised teams and standardised workflows in transplant medicine.

P52 IMPACT OF IMMORTALIZATION FOR ESTABLISHMENT OF HEPATOCYTE-LIKE CELLS

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Introduction and Background: Hepatocyte-like cells (HLC) generated from induced pluripotent stem cells (iPSC) offer great opportunities to study diseases in a patient-specific manner. Urine-derived cells (UCs) are an easy attainable source of primary cells and can be used for the generation of iPSC. Unfortunately, like primary hepatocytes, HLC do not proliferate in vitro and consecutive differentiations are time consuming. The use of genes reported to immortalize cells could boost the current protocols of HLC generation. We wanted to investigate whether transfer of genes mediating immortalization modulates the process of reprogramming and differentiation.
Methods: Retroviral transduction using various gene combinations was performed at different stages of reprogramming and differentiation. Cells were transduced with hTERT/p53, CyclinD1/CDK4, and HPVE6E7 or combinations thereof. The influence of gene transfer was assessed by determination of cell proliferation, mRNA expression (qRT-PCR) and protein expression (e.g. flow cytometry, immunofluorescence).
Results and Conclusions: Untreated or GFP transduced UCs underwent senescence after 5–10 days. In contrast, UCs could be cultured for several months in the presence of HPVE6E7 (UCim; $n = 3$). Expression of renal, epithelial and fibroblast marker genes in UCs and UCim was in the same range. Using a transient, EBV-based expression system for reprogramming, UCim could be reprogrammed to iPS cells that expressed typical markers of pluripotency. However, reprogramming of UCim resulted in less iPSC-like colonies (iPSCim) and was delayed. The expression of hepatic markers was assessed after hepatic differentiation of UCim (HLCim). Expression of transgenes was downregulated after reprogramming to iPSCim and differentiation to HLCim.

P53 OUTCOME FOLLOWING RIGHT-EXTENDED SPLIT LIVER TRANSPLANTATION IN THE RECENT TRANSPLANT ERA – SINGLE CENTER ANALYSIS

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Introduction and Background: In case of allocation of the graft to a small child classic liver graft splitting is performed with consecutive transplantation of the right-extended liver in an adult. Based on organ quality data a clearly superior outcome following split liver transplantation (LTX) should be expected, especially in contrast to the decreasing donor quality in Europe since implementation of the MELD allocation system.
Methods: We analyzed our recipients of right-extended grafts regarding donor/recipient data and outcome (2007–2015). Special regard was given to the splitting procedure (in-house liver graft splitting by the own team versus external liver graft splitting by a different team with subsequent graft shipping).
Results and Conclusions: We found excellent donor data with hemodynamic stable donors (short ICU stay (3 ± 3 days), low maximum catecholamine level (0.2 ± 0.2 μg/kg/min), low reanimation rate (23%)) of a young age (28 ± 13 y) with normal or at most slightly elevated liver enzymes. Recipient characteristics were comparable between patients with in-house versus external liver graft splitting, however cold ischemic time was significant longer in external liver graft splitting (14 ± 2 versus 12 ± 2 h). Interestingly, there was a significant reduced patient and a clear trend to a reduced graft survival with external liver graft splitting. Likewise the rate of biliary and vascular complications was higher in patients with external versus in-house liver graft splitting (21% and 12% versus 8% and 0%).

In our study we found a negative impact of external liver graft splitting on the outcome and surgical complications. This may related to the prolonged cold ischemic time due to twofold transportation and the ignorance of the detailed splitting procedure and pitfalls.

P54 HOW DO MTOR INHIBITORS MODULATE HCV REPLICATION ACTIVITY: AN APPROACH BY WHOLE GENOME ANALYSIS

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Introduction and Background: Hepatitis C virus (HCV) infection remains an important cause for liver transplantation (LT) and reinfection of the liver graft is a serious challenge. The influence of mTor inhibitors as immunosuppression (IS) after LT on HCV replication activity and, thus, reinfection of the graft, has not been elucidated so far. We could previously show that mTor inhibitors (everolimus (EVR), sirolimus (SRL)) exert genotype (GT)-dependent effects on HCV replication activity. Aim of this study is to investigate the molecular background of this differential effect.
Methods: GT1b (Con1) and GT2a (Huh7.5 JFH/SG-Feo) replicon cells were treated with mTor inhibitors and the gene expression profile was generated using GeneChip® Human Transcriptome Array 2.0. Those genes, which showed a differential regulation between HCV genotypes, were further analysed by qRT-PCR.
Results and Conclusions: As genes of interest were those selected which were previously described in the context of viral hepatitis: cyclin T1 (CCNT1), the transcription factor E2F2 and the hepatitis A virus cellular receptor 1 (HAVCR1). Treatment of GT2a cells with either mTor inhibitor resulted in 1.5-fold higher CCNT1 expression (EVR: $p \leq 0.005$, SRL: $p \leq 0.05$) and 2-fold increase in E2F2 expression (EVR / SRL: $p \leq 0.05$) compared to the untreated control while there was no change in expression of these two genes in GT1b cells. HAVCR1 was reduced by 0.5-fold in the GT1b cells by EVR or SRL treatment (EVR: $p \leq 0.005$, SRL: $p \leq 0.0001$). In contrast, there was no effect on the regulation of this gene in the GT2a cells. In conclusion, we could identify a highly significant difference in regulation of CCNT1, E2F2 and HAVCR1 between HCV-GT1b and GT2a cells upon mTor inhibitor-treatment. These factors are likely to play a central role in regulation of HCV replication activity by mTor inhibitors and are currently under further investigation.

P55 TRANSPLANTATION OF STEATOTIC LIVERS – AN INCREASING PROBLEM WITH SEVERE COMPLICATIONS

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Introduction and Background: The rising prevalence of the metabolic syndrome will lead to increased numbers of liver grafts with steatosis hepatitis, an important risk factor for graft dysfunction after liver transplantation. We evaluated the impact of steatosis hepatitis on graft acceptance rate and on the outcome after liver transplantation in a German high-volume center.
Methods: Non-acceptance of liver offers to the Charité – Universitätsmedizin Berlin between 2010 and 2016 were examined and classified. All available case files were screened for pre-transplant histopathological analysis of the graft. Macrovesicular steatosis was classified into <5% (S0), <30% (S1), <60% (S2) and ≥60% (S3). Early allograft dysfunction (EAD), graft and recipient survival were correlated with the degree of steatosis hepatitis of the graft. The survey was approved by the local ethical board.
Results and Conclusions: Steatosis hepatitis accounted for up to 15% of medical non-acceptance. In 2010, 15 offers were rejected due to steatosis, while 103 liver transplants were performed. In 2015, 28 offers were rejected due to steatosis, while 78 transplants were performed. After transplantation of S1, S2 & S3 grafts serum transaminases were significantly higher at POD 1 ($p \leq 0.0001$), POD 2 ($p = 0.019$) and POD 4 ($p = 0.039$). EAD significantly increased ($p = 0.013$) with higher degrees of graft steatosis: S0 (21.3%), S1 (39%) and S2&3 (56.3%). Cold ischemic time (CIT) >8 h and S1, S2 or S3 led to EAD in 70.3% of cases compared to 29.7% without long CIT. EAD was a predictor of 1-year recipient ($p \leq 0.0001$) and graft survival ($p \leq 0.0001$) and remained a significant predictor in multivariate analysis of 1-year recipient ($p = 0.035$) and graft survival ($p = 0.021$).

Steatosis hepatitis is a rising problem that increasingly limits the success of liver transplantation. New concepts are necessary to address this problem, from limiting the effects of CIT to conditioning steatotic liver grafts prior to transplantation.

P56 IMPACT OF BRIDGING THERAPY ON THE SURVIVAL AND RECURRENCE RATE AFTER LIVER TRANSPLANTATION FOR HCC

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Introduction and Background: Tumor recurrence is a frequent cause of death after liver transplantation (LTX) for HCC. We investigated the impact of the bridging therapy (BT) on the long-term survival and the tumor recurrence rate.
Methods: We analyzed 147 consecutive adult patients who underwent transplantation between 1996 and 2014 and who survived for at least 3 months. Bridging therapies were TACE, RFA and SIRT. The cumulative survival rate (CSR) and recurrence rate (CRR) were calculated according to Kaplan-Meier. The median follow-up period is 48 months.
Results and Conclusions: 70 patients (48%) received a bridging therapy. 48 (33%) developed a recurrence. The median survival of all patients was 106 months. The observed 5 and 10 years CSR after LTX was 61% and 43%, respectively ($p = 0.016$). None of the 18 patients without evidence of a tumor in the explant specimen developed a recurrence. Significant impact on the CRR had among others BT ($p = 0.005$), Milan ($p = 0.008$) and Duvoux score ($p < 0.001$). With stratification according to Milan the impact of the BT on the CRR was maintained: (inside Milan 11% vs. 32%, $p = 0.058$; outside Milan 31% vs. 57%, $p = 0.025$). The BT influenced the location of the tumor recurrence: following BT intrahepatic recurrences were less frequently observed (1% vs. 22%, $p < 0.001$), extrahepatic recurrences approximately equal in frequency (23% vs. 32%, $p = 0.407$). The CSR after extrahepatic recurrence was better than after intrahepatic recurrence ($p = 0.001$).

With BT in HCC, long-term survival, CRR and location of the tumor recurrence after LTX are positively influenced.

P57 PERIVASCULAR INFILTRATION OF LYMPHOCYTES INFLUENCE OF THE DISEASE-FREE SURVIVAL AFTER RESECTION OF HEPATOCELLULAR CARCINOMA

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Introduction and Background: Liver resection is a potentially curative treatment option for hepatocellular carcinoma. Tumor recurrence is frequent because it does not remove the liver as precancerosis. Aside from the liver cirrhosis is therefore dependent on biology of the tumor cells and the immunological reaction they provoke. This immunological reaction has been the subject of intense research in recent years. Both the innate and adaptive immune system play an important role in the tumoricidal reaction of the immune system. In here we present the results of an experimental study examining the type, density and location of tumor infiltrating leukocytes (TILs) from the innate and the adaptive immune system.
Methods: 60 patients of the tumor material were accessed. Immunohistochemistry was performed against CD3, CD8, CD20 and CD66b. TILs were counted with the quantification of tumor stroma in the perivascular (PV) regions. High and low infiltration groups was defined by medians. PV regions were defined as the accumulation of lymphocytes around the intratumoral vessels. Results were correlated with overall (OS) and disease-free survival (DFS).
Results and Conclusions: The perivascular CD8 + T cells densities strongly correlated with CD20 + B cells ($r = 0.856$, $p < 0.001$). The perivascular CD66b + neutrophil-like correlates with preoperative circulating leukocytes ($r = 0.343$, $p = 0.007$), platelets ($r = 0.420$, $p = 0.001$), and C-response protein ($r = 0.344$, $p = 0.008$). No evidence was found for the influence of CD3 ($p = 0.058$), CD8 ($p = 0.297$), CD20 ($p = 0.535$), or CD66b ($p = 0.616$) on OS. Higher perivascular infiltration of CD3 ($p = 0.016$) and CD8 (0.028) significantly predicted better DFS. The CD20 ($p = 0.076$) and CD66b ($p = 0.521$) had no significant influence on DFS.

Perivascular infiltrating lymphocytes predict disease-free survival of patients undergoing curative resection.

P59 LONG TERM OUTCOME AFTER ENDOSCOPIC TREATMENT OF ANASTOMOTIC AND NON-ANASTOMOTIC BILIARY STRICTURES IN LIVER TRANSPLANT RECIPIENTS

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Introduction and Background: Biliary tract complications (BTC) are the leading problem in patients after orthotopic liver transplantation (LTx). The present study analysed the predictors of treatment outcome in patients with biliary stenoses undergoing endoscopic retrograde cholangiopancreatography (ERCP) and/or percutaneous transhepatic cholangiodrainage (PTCD) at the University Medical Center Hamburg-Eppendorf.
Methods: All adult patients who received ERCP or PTCD for BTC after LTx between 2009 and 2015 were retrospectively analysed. Remission was defined as no need of intervention for at least 12 months. To identify predictors of treatment outcome in patients with biliary stenoses, a multivariate logistic regression analysis was performed after univariate variable selection. Furthermore, interventional techniques were analysed in the ERCP- and PTCD-subgroup.
Results and Conclusions: Of 144 patients with BTC after LTx, 116 were diagnosed with stenoses. Among these, 86 received ERCP, 17 PTCD and 13 both. Long-term remission was achieved in 55 patients (47% overall; 53% with ERCP only and 30% with PTCD treatment). Patients with non-anastomotic stenoses (NAS) (odds ratio [OR] 0.25, 95% confidence interval [CI] 0.10–0.55; $p = 0.001$), requirement of PTCD (OR 0.30, 95% CI 0.10–0.79; $p = 0.018$) and higher pre-interventional bilirubin (OR 0.88, 95% CI 0.76–0.98; $p = 0.037$) were less likely to achieve remission. In the ERCP-subgroup, dilation with a higher maximal balloon-diameter was associated with a favourable outcome ($p = 0.043$). In conclusion, both ERCP and PTCD can provide long-term benefit in patients with BTC after LTx. Patients with NAS, requirement of PTCD and higher bilirubin may have a higher risk of treatment failure. Larger ERCP balloon diameters may favour remission.

P61 (EXTENDED) RIGHT SPLIT LIVER TRANSPLANTATION - AN ANALYSIS FROM THE EUROTRANSPLANT LIVER FOLLOW-UP REGISTRY

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Introduction and Background: Split liver transplantation (SLT) has been perceived as an important strategy to increase the supply of liver grafts by creating 2 transplants from 1 allograft. The Eurotransplant allocation system (ELAS) envisages that the (E)RLs after splitting (usually in the pediatric center) are almost exclusively shipped to a second center. Whether the ELAS policy impacts the graft and patient survival of (E)RLT in comparison to WLT recipients remains unclear.
Methods: Data on all LTs performed between 2007 and 2013 were retrieved from the ET Liver follow-up Registry ($n = 5351$). Data on $n = 5013$ (269 (E)RL, 4744 WL) could be included. The impact of the transplant type on patient and transplant survival was evaluated using uni- and multivariate proportional hazard models adjusting for demographics of donors and recipients.
Results and Conclusions: Cold ischemia times (CIT) were significantly prolonged for (E)RLTs ($p < 0.001$). Patient survival was not different between (E)RLT and WLT. In the univariate analysis (E)RLT had a significantly higher risk for retransplantation ($p = 0.021$). For WLT the risk for death gradually and significantly increased with labMeld-scores of >20. For (E)RLT this effect was seen already with labMELD scores of >14.

Within ET, (E)RLT results in a higher retransplantation rate but similar survival compared to WLT. Our results suggest that (E)RLT outcome could be further improved by an allocation algorithm allowing for short CIT and an optimized (E)RLT/recipient match.

P62 HEPATIC ARTERY AND BILIARY COMPLICATIONS IN LIVER TRANSPLANT RECIPIENTS WITH RADIOEMBOLIZATION BRIDGING TREATMENT FOR HEPATOCELLULAR CARCINOMA

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Introduction and Background: Locoregional bridging treatments are commonly applied in hepatocellular carcinoma (HCC) patients prior to liver transplantation to prevent tumor progression during waiting time. It remains unknown whether pre-transplant radioembolization treatment may increase the prevalence of hepatic artery and biliary complications post-transplant.
Methods: We performed a retrospective review of 173 consecutive HCC patients who underwent liver transplantation at our transplant center between January 2007 and December 2016. The prevalence of hepatic artery and biliary complications in patients treated with and without radioembolization prior to liver transplantation was compared. Possible risk factors associated with hepatic artery and biliary complications were evaluated using simple and multivariable logistic regression.
Results and Conclusions: Radioembolization bridging treatment was applied in 42 patients while 131 patients received other or no forms of bridging treatment. The overall prevalence of intraoperative and early postoperative hepatic artery complications was 9.5% in the radioembolization group and 9.2% in the control group ($p = 1.000$). Biliary complications were significantly less frequent in the radioembolization group (4.8% vs. 17.6%, p 0.0442). In multivariable analysis, radioembolization was not significantly associated with an increased risk of arterial complications. Considering biliary complications, radioembolization bridging treatment was the only factor significantly associated with decreased odds (OR 0.187 (0.039, 0.892), $p = 0.036$).

Radioembolization is not associated with higher odds of hepatic artery complications following liver transplantation. There may even be a protective effect regarding biliary complications. Radioembolization as a bridge to transplantation may effectively be applied without compromising successful liver transplantation.

P63 CLINICAL PREDICTORS FOR TREATMENT COSTS PER SURVIVED DAY AFTER LIVER TRANSPLANTATION AND OPTIMIZED RESOURCE ALLOCATION

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Introduction and Background: Liver transplantation belongs to the most expensive medical treatments. The aim of this study was to identify independent risk factors for resource utilization after liver transplantation.
Methods: Treatment expenses in Euros per survived post-transplant day (€/d) of 182 patients were analyzed. Multivariable logistic regression models were determined and their prognostic capability for predicting highest and lowest post-transplant costs evaluated using areas under the receiver operating characteristic curve (AUROCs).
Results and Conclusions: Lowest €/d were predicted with the recipient hemoglobin level ($p < 0.001$; odds ratio (OR): 1.242, 95%-confidence interval (95%-CI): 1.157–1.622), donor age ($p = 0.01$; OR: 0.964, 95%-CI: 0.938–0.991), donor quick value ($p = 0.02$; OR: 13.678, 95%-CI: 1.470–127.253), donor bilirubin level ($p = 0.047$; OR: 0.931, 95%-CI: 0.868–0.999) and the amount of macrovesicular steatosis of the liver graft ($p = 0.02$; OR: 0.761, 95%-CI: 0.601–0.964). This model displayed an AUROC of 0.77 for the prediction of the lowest €/d. Highest €/d were predicted with the recipient age ($p < 0.001$; OR: 1.072, 95%-CI: 1.027–1.120), MELD-score ($p = 0.002$; OR: 1.052, 95%-CI: 1.017–1.088), primary sclerosing cholangitis ($p < 0.001$; OR: 0.039, 95%-CI: 0.004–0.381), donor ventilation time ($p = 0.011$; OR: 1.004, 95%-CI:1.001–1.007), donor creatinine level ($p = 0.03$; OR: 1.003, 95%-CI: 1.000–1.006), a performed hepaticojejunostomy ($p < 0.001$; OR: 9.919, 95%-CI: 3.057–32.184) and multiple arterial anastomoses ($p = 0.048$; OR: 3.276, 95%-CI: 1.031–10.406). This model displayed an AUROC of 0.81.

Pre-operative donor and recipient and transplant specific variables can predict treatment costs per survived day after liver transplantation. The introduced index in €/d can enable benchmarking between transplant centers and result in an improved distribution of monetary resources and donor grafts.

P64 CLINICAL AND LABORATORY FEATURES CAN PREDICT SURVIVAL OF PATIENTS WITH BUDD-CHIARI SYNDROME AFTER LIVER TRANSPLANTATION

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Introduction and Background: Budd-Chiari syndrome (BCS) is a rare but critical condition that can progress to liver failure and death. For severe cases orthotopic liver transplantation (OLT) remains the only curative option. Though, currently no factors to predict prognosis after OLT for BCS are available. The present study aimed to identify predictive parameters to assess possible outcome prior OLT.
Methods: Patient data from 33 individuals with BCS who received an OLT were retrospectively assessed. 27 eligible patients were identified, which were grouped by outcome after OLT into survivors (group 1; $n = 18$) and deceased (group 2; $n = 9$). Demographic, clinical, and serum parameters taken at the time of BCS diagnosis were evaluated for prognostic value.
Results and Conclusions: Clinical and serum parameters indicated an impaired liver synthesis and detoxification capacity, liver parenchyma damage and clear signs of inflammation in BCS patients at diagnosis. Differences between group 1 and 2 were found for nausea/vomiting ($p < 0.01$) and splenomegaly ($p < 0.01$), which were both more common in patients, who deceased after OLT. In addition patients of group 2 exhibited significantly lower serum cholinesterase ($p < 0.01$) and higher alkaline phosphatase ($p < 0.01$). Scoring systems to assess liver status or BCS severity (MELD, Child-Pugh-Score, Rotterdam Score, BCS-TIPS-PI) did not differ between the groups. The symptoms nausea/vomiting, splenomegaly and low serum cholinesterase as well as high alkaline phosphatase are associated with adverse outcome after OLT for BCS. These factors might be surrogate markers for a severely impaired health status at time of diagnosis and should be evaluated prospectively in larger cohorts.

P65 INFLUENCE OF TERLIPRESSIN ON ARTERIAL AND BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION

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Introduction and Background: Hyperdynamic portal venous perfusion after liver transplantation (LT) for cirrhosis decreases the grafts" arterial perfusion via mechanisms including the arterial buffer response. The biliary system is highly dependent on arterial flow. Thus this study was designed to investigate the effect of terlipressin on both arterial and biliary complications after LT.
Methods: Terlipressin was given based on the surgeons" interpretation of both the portal venous and arterial flow. A retrospective matched pair analyses was performed with a total number of 86 patients who underwent LT with and without post- and/or intraoperative terlipressin. The matching was performed based on the recipients" age and MELD score. The patients" general condition and both the arterial and biliary complication rates during the postoperative hospital stay were compared between groups.
Results and Conclusions: Intraoperative terlipressin decreased the portal venous flow while the arterial flow was improved; however, the impact of terlipressin on both the arterial and biliary complication after LT yet was not significant.

While terlipressin nicely improved the grafts" arterial perfusion no significant effect on both arterial and biliary complications were detected. Since conclusions from a retrospective matched pair analysis are limited the pros and cons of terlipressin must be critically reflected. RCTs are warranted to elucidate the further potentials, indications and dosing regimens of terlipressin in the transplantation setting.

P66 INCISIONAL HERNIA REPAIR IN PATIENTS AFTER LIVER TRANSPLANTATION WITH POLY-4-HYDROXYBUTYRATE MESH

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Introduction and Background: Incisional hernia is a common problem after liver transplantation (LT). Permanent mesh implantation has a risk of chronic infection in immunosuppressed patients. Poly-4-Hydroxybutyrate (P4 HB) commonly used as ultra-slow absorbable suture material is now considered for new generation of absorbable synthetic mesh. Most recently excellent results with P4 HB mesh in complex infected hernia have been observed. Thus

incisional hernia repair after LT with P4 HB mesh in patients after LT has been implemented.
Methods: In 2016 five patients after LT underwent onlay-enforcement closure of incisional hernia with P4HB mesh together with P4HB thread in a running suture and small bites technique.
Results and Conclusions: All patients had uneventful wound healing, supported by a negative pressure suction device of −100 mmHg applied on the closed wound for five days. The follow-up period was between four and eleven months. All patients remained without complications and discomfort.

Onlay-enforced closure of incisional hernia after LT is a safe procedure. To confirm our data a RCT should be performed. Based on this observational trial a RCT would be warranted.

P67 UTILITY OF RETROSPECTIVE TWO ONE-SIDED CUMULATIVE SUM CHARTS COMBINED WITH MULTIVARIABLE REGRESSION ANALYSIS FOR QUALITY ASSESSMENT IN LIVER TRANSPLANTATION

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Introduction and Background: This study investigated the utility of retrospective two one-sided cumulative sum (CUSUM) charts combined with multivariable regression analysis in liver transplantation for transplant centre benchmarking.
Methods: 1749 consecutive adult primary liver transplants (01.01.1983–31.12.2012) were analysed retrospectively with two one-sided CUSUM chart analysis of 90-day mortality.
Results and Conclusions: Three eras and two subseries in latest era 3 were identified due to graphically delineated relevant shifts in mean 90-day mortality. Delineation of eras 1, 2 and 3 coincided with relevant changes in allocation policies. CUSUM analysis detected a resurgence of higher mean 90-day mortality in era 3 after results had improved continuously over 25 years. In era 3, two subseries were identified with improving mean 90-day mortality rates from 15.4% in subseries 1 to 8.9% in the following subseries 2. The quantitative influence of independent risk factors on 90-day mortality differed markedly between all identified eras and subseries as assessed with multivariable regression analysis deployed on era-specific subcohorts. The assessed methodology is able to identify meaningful centre-specific eras and subseries of liver transplantation with striking alterations of the significance and weight of outcome drivers for post-transplant 90-day mortality over time. This warrants the introduction of prospective risk-adjusted two one-sided CUSUM chart analysis into quality management in liver transplantation in Germany with the goal to obtain alarm signals as early as possible.

P68 LOW SHORT TERM ASAT AFTER LIVER TRANSPLANTATION PREDICTS GOOD LONG TERM OUTCOMES

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Introduction and Background: Prediction of long-term prognosis after orthotopic liver transplantation (OLT) remains difficult.
Methods: This retrospective study aimed to identify predictors of stable long-term outcome analysing standard laboratory parameters such as ASAT and ALAT at different time points after OLT.
Results and Conclusions: 190 matched patients after OLT from 1987–2013 with 1-27 years of follow up were included to the study. Short-term survivors (group A; <5 years) and patients with mid-term survival of 5-10 years (group B) were compared to 29,5% patients with long-term survival >10 years (group C). Median ASAT and ALAT levels 7 days, 90 days, 1,2,3,5,7,9 and 10 years after OLT of group C were compared to group A/B. Median ASAT and ALAT levels of group C showed a notch 90 days after OLT. Further statistical analysis of ASAT levels 90 days after OLT revealed a median value of 16 U/ml in group C and 102 U/ml in group A/B. Median AST 90 days after OLT of group C was significantly lower in group A/B when performing survival analysis with the combined end point "death or re-OLT" ($p = 0.005$). For ALAT, statistical analysis indicated a significantly ($p = 0.012$) lower median value in group C (20 U/ml) compared to group A/B (109 U/ml).

In conclusion low ASAT levels 90 days after OLT predicts a good clinical long-term outcome.

P70 LIVER TRANSPLANTATION FOR ALCOHOLIC HEPATITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and Background: Early liver transplantation (LT) to rescue patients with severe alcoholic hepatitis unresponsive to medical therapy remains controversial. Furthermore, recent studies questioned the role of the required six-month alcohol abstinence prior to transplantation. The aim of this review is to gain evidence on liver transplantation (LT) in patients with acute alcoholic hepatitis regarding overall survival and alcoholic relapse compared to control.
Methods: Any study type comparing patients with alcoholic hepatitis undergoing LT with a control group was included. CENTRAL, MEDLINE and Web of science were searched. Meta-analyses were performed with a random-effects model calculating odds ratio (OR) with 95% confidence intervals at a level of significance of 5%.
Results and Conclusions: We identified nine studies. For them two different meta-analyses were performed. In two studies early LT for patients with severe alcoholic hepatitis not responding to medical therapy were compared to medical therapy, the six-month patient survival (OR 15; $p < 0.00001$) and one-year patient survival (OR 5.9; $p = 0.001$) were significantly higher in the transplantation group. Seven studies compared LT for patients with alcoholic hepatitis failing the 6-month abstinence with LT for alcoholic liver disease without acute hepatitis. One-year survival (OR 1.4; $p = 0.15$), three-year survival (OR 1.5; $p = 0.08$) and five-year survival (OR 1.4; $p = 0.15$) was not different between the groups. Alcohol relapse was also not significantly different in groups (OR 1.9; $p = 0.08$).

Early LT should be considered as a life-saving treatment for selective patients with alcoholic hepatitis not responding to medical therapy. The quality of evidence is moderate and based on the results of two prospective case-control studies. Future randomized controlled trials taking into consideration long time survival and alcohol relapse are needed to ensure comparability and effectivity of results.

P71 HIGH COST CASES IN LIVER TRANSPLANTATION - A RETROSPECTIVE INTER-SECTORIAL ANALYSIS OF COST RISING FACTORS

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Introduction and Background: The treatment process of liver transplantation (LT) is known to be very resource intensive. Identification of economic cost drivers is essential to target optimization of resource utilization and allocation. The aim of this study is to identify variables that rise costs significantly for the outpatient, inpatient and rehabilitative health care sectors as well as for medications.
Methods: We retrospectively evaluated data about resource utilization for LT-patients ($n = 182$) between 01.01.2010 and 31.12.2015. Current reimbursement schemes were used for cost calculation taking the perspective of statutory health insurance organizations. Quartiles of treatment costs were used to identify high cost cases in the fourth quartile. The influence of clinical variables on high cost cases was analyzed using univariable and multivariable logistic regression modeling.
Results and Conclusions: Outpatient costs rise significantly with the number of days on the waiting list and the observational time. During hospitalization for TX the MELD-Score as well as death after TX or subsequent re-TX have been identified as significant cost drivers. The indication of acute liver failure and the ration of receiver BMI divided by donor BMI >1.104 have a significant influence on high costs cases during rehabilitation. Recipient age, donor age and death after TX are significant variables for high spending on immunosuppressive drugs. Overall costs for other medications are significantly higher for patients with viral cirrhosis and liver malignancy. These results provide an adequate basis to set incentives for different forms of compensation. Significant economic process optimization would be expected by the reduction of waiting times prior to TX, the prevention of re-TX and death after TX and a better balance between recipient and donor BMIs in organ allocation.

P72 PREDICTION OF CHRONIC KIDNEY DISEASE AFTER LIVER TRANSPLANTATION

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Introduction and Background : After liver transplantation, several complications have an impact on patients" life. Among those, occurring chronic kidney disease (CKD) is well known for its impact on mortality and morbidity. This study explores the incidence and possible risk factors for development of chronic kidney diseases in patients without pre-existing renal comorbidities prior to transplantation.
Methods: Adult liver transplant patients (n = 470) without pre-existing chronic kidney diseases were analyzed. All patients had received their first liver transplantation. Endpoint was the occurrence of chronic kidney disease with KDIGO stage ≥3 one year after transplantation. Clinical data and comorbidities of recipients as well as data from organ donors, transplant operation and subsequent clinical complications were used to generate four separate models by multivariable binary logistic regression.
Results and Conclusions: New chronic kidney disease KDIGO ≥3 occurred in 70 (14.9%) patients within one year after transplantation. Models with robust AUROCs can be computed by meta-modeling (AUROC 0.8113) or combining independently significant variables directly (AUROC 0.8155). Higher recipient age (52 vs. 45 years; OR 1.053), lower preoperative hemoglobin (10.7 vs. 11.8 mg/dl; OR 0.821), higher BMI (27 vs. 25 kg/m²; OR 1.117) as well as comorbidity groups weight loss (10% vs. 3%; OR 6.436) and pulmonary circulatory disorder (10% vs. 2%; OR 6.268) increase risk for CKD. Hepaticojejunostomy (7% vs. 25%; OR 0.225) and pre-existing hypothyroidism (1% vs. 6%; OR 0.097) decreased the risk.

The identification of patients at high risk to develop CKD is essential to adjust potentially nephrotoxic immunosuppression as well as other treatment. Factor interactions may have to be taken into account in future analyses.

P73 INTRODUCTION OF A PROGNOSTIC MODEL FOR 90-DAY MORTALITY AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Introduction and Background : This study aims to propose a prognostic model for 90-day mortality after liver transplantation for patients transplanted due to hepatocellular carcinoma (HCC).
Methods: A total of 173 patients (age>17 years) transplanted with the indication HCC were analysed. Computing the multivariable logistic regression model, potential non-additional factor interactions and possible nonlinear influences of continuous variables were taken into account.
Results and Conclusions: Following preoperative donor variables were detected as significant risk factors by multivariable logistic regression: macrovesicular steatosis (%) (p = <0.001, OR = 1.151, 95%-CI = 1.060–1.250) and dobutamine (p = 0.015, OR = 5,156, 95%-CI = 1.486–17.890). A multiplicative factor interaction between the positive donor Rhesus factor and the donor temperature (p = 0.036, OR = 0.969, 95%-CI = 0.942–0.997) was discovered after purposeful selection of covariates.

Intra- and postoperative prognostic factors for 90-day mortality were duration of operation (p = 0.009, OR = 1.008, 95%-CI = 1.002–1.014) and the occurrence of surgical complications (p = 0.001, OR = 5.896, 95%-CI = 1.966–17.684). These results are independent of the transformation of continuous variables using spline functions and knots.

Results suggest that organs from donors with a high percentage of macrovesicular steatosis of the liver carry a high risk of 90-day mortality after transplantation for HCC. Administration of dobutamine to donors before donation also increases this risk. In current literature, no information describes the relation between a rhesus positive donor and his temperature. This requires further targeted investigations, including a pending external validation. Duration of operation and surgical complications commonly suggest higher levels of intraoperative difficulty and thus increase the likelihood of 90-day mortality after liver transplantation in patients with HCC.

PANCREAS

P74 LONG-TERM RESULTS FOLLOWING ALEMTUZUMAB VERSUS ATG INDUCTION THERAPY IN COMBINED KIDNEY-PANCREAS TRANSPLANTATION: A SINGLE CENTER REPORT

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Introduction and Background: A retrospective long-term analysis of patient and graft survival, graft function and major complications following induction therapy with Alemtuzumab versus ATG in simultaneous pancreas kidney transplantation (SPK).
Methods: A historical study cohort of totally 14 SPK randomized to Alemtuzumab plus Tacrolimus-monotherapy (group A) versus 16 SPK with ATG plus Tacrolimus, MMF and steroids (group B) performed at our center between 2006 and 2010, was retrospectively analyzed within a mean follow up period of 9.5 years post transplant.
Results and Conclusions: The 9 years survival of patients in group A/B was 92.9%/86.7%, of pancreatic graft 90.9%/81.3 %, and renal graft 83.1%/93.8. The causes of death were tumor, sepsis (group A), cerebrovascular accident and unknown reason (group B). In the surviving grafts the mean longterm creatinine (mg/dl) in group A/B was 2.1/1.3, fastening glycaemia (mg/dl) 86.4/70.2, HbA1c (g%) 5.7/6.0. Apart from 4 fatal complications mentioned, all other major complications in both groups without statistically significant difference, were controllable. One fatal malignancy occurred in group A and three (all survived) in group B.

Good long-term results in patient, pancreas and kidney graft survival were achieved in both groups with comparable graft function and incidence of major complications. More tumors occurred in group B, all survived, in contrast to one fatal malignancy in group A.

THORACIC ORGANS

P77 SINGLE CENTER ANALYSIS OF POSTOPERATIVE COMPLICATIONS AFTER HVAD IMPLANTATION

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Introduction and Background: A third-generation ventricular assist device, the HeartWare Ventricular Assist System, has demonstrated its reliability and durability in clinical experience. However, relatively few studies have examined the full spectrum of complications after HVAD implantation beyond infectious and bleeding events.
Methods: We conducted a retrospective review of 104 patients receiving 3rd generation continuous flow, centrifugal blood pump HeartWare ventricular Assist device HVAD® (HeartWare, Inc., Framingham, Massachusetts) at the department of thoracic organ transplantation, University Hospital Essen, Germany. The study was conducted between August 2010 and March 2015. Frequency and date of onset of postoperative complications in relation to INTERMACS scale were examined.
Results and Conclusions: Overall, the most frequent complications were sepsis (47.1%), right ventricular failure (37.5%) and respiratory failure (33.7%). Within one postoperative week, renal failure was the most common complication followed by right ventricular failure and respiratory failure. Complications that were common between one week and one month postoperatively were sepsis, respiratory failure and right ventricular failure. Stroke was a late complication which occurred most frequently after 6 months. INTERMCAS profile 1 had a significant higher incidence of postoperative respiratory failure (p = 0.013), surgery related hemorrhage (p = 0.029) and multiorgan failure (p = 0.014) in comparison to other INTERMCAS profiles.

In this 5-year review, the most common adverse events tended to occur early after HVAD implantation. Preoperative INTERMCAS classification correlates with postoperative complications.

P78 A THIN LINE LINE BETWEEN REJECTION AND BK VIRUS INFECTION AFTER HEART TRANSPLANTATION

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BK virus (BKV) infection is a sign of over-immunosuppression, however optimal therapy of harmful BKV infections after HTx remains unclear. Here we present an unusual case of BKV infection in a patient with rejection.

Our 32 years old HTx patient suffered from severe cytomegalovirus (CMV) pneumonia induced sepsis and developed renal failure after 4 months. At month 6 the patient had sudden onset of impaired graft function. Cellular-mediated rejection (CMR) was verified by biopsy (ISHLT 2R) and antibody-mediated rejection (AMR) by detection of donor specific antibodies, ultrasound results and clinical symptoms. Rejection therapy was performed with methyl-prednisolone pulse therapy, 4 cycles of plasmapheresis, immunoglobulin and rituximab. While graft function recovered renal impairment deteriorated further requiring dialysis with evidence of BK viruria first (copies max. 1x109) and BK viremia (copies max. 7000) later. Consequently, we added leflunomide, administrated CMV-IgG (cumulative 40.000 IE / 6 weeks) which also contains antibodies against BKV, lowered Tac-levels (6–8 to 4–6 ng/ml) and stabilized everolimus (ERL) levels (3–8 ng/ml). Under this treatment RF recovered to almost normal (creatinine 1.6 mg/dl), BK viruria could be reduced (copies min. 2 × 108) and viremia of BKV vanished.

Our case demonstrates how thin the line is between intense and reduced immunosuppression to treat rejection and BKN, respectively. Adding leflunomide and high doses of CMV-IgG to low TAC- and normal ERL-levels may help to treat BKV infection. However, detection of BKV in patients with either anti-rejection therapy or new onset of nephropathy should become a standard after HTx.

P79 2-YEAR FOLLOW-UP AFTER MINIMALLY-INVASIVE LEFT VENTRICULAR ASSIST DEVICE IMPLANTATION - A SINGLE CENTER EXPERIENCE

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Introduction and Background: Implantation of minimally-invasive left ventricular assist device (mLVAD) avoids a full sternotomy, probably reducing the surgical risk of following transplantations or right ventricular (RV) failure. We demonstrate our results of mLVAD implantation (mLAVD) operated via left lateral thoracotomy compared to LVAD implantation (LVAD) done via full median sternotomy.
Methods: Data of 70 patients (mLAVD $n = 22$, 52 ± 15 years; LVAD $n = 48$, 59 ± 11 years), who received a HVAD system (HeartWare®) between 2010 and 2015 were analysed retrospectively.
Results and Conclusions: 31.8% (7/22) of mLVAD and 56.3% (27/48) of LVAD were classified as INTERMACS level I/II, whereas 68.2% (15/22) of mLVAD and 43.7% (21/48) of LVAD belonged to INTERMACS level III/IV. In 81.8% (18/22) of the mLVAD the outflow graft was anastomosed to the ascending aorta via right minithoracotomy ($n = 14$) or hemisternotomy ($n = 4$); while 18.2% (4/22) were anastomosed to the descending aorta. Cardiopulmonary bypass was initiated percutaneously into the femoral vessels, 40.9% (9/22) of the mLVAD received a temporary RV support (tRVAD) due to reduced RV-function.

The mLAVD presented a 2-year survival of 59.1%, non-significant superior compared to the LVAD with 47.9% ($p = 0.62$). 6 patients were transplanted during follow-up (mLVAD 2/22, LVAD 4/48) and 3 LVAD-patients were able to be weaned with successive LVAD explantation. A tendency towards less LVAD-specific infections was found in mLVAD ($p = 0.06$). Multiple organ failure was the most common cause of death (mLVAD 3/22, LVAD 12/22). Significant superior survival was seen in patients receiving mLVAD without tRVAD related to patients with LVAD/tRVAD implantation ($p = 0.022$). During the 2-year follow-up RV-failure occurred in 9.1% (mLVAD 2/22) compared to 10.4% in LVAD (5/48) ($p > 0.05$).

MLVAD implantation is a feasible technique and is non-inferior compared to sternotomy and particularly suitable for bridge-to-transplant patients. For prediction and avoidance of RV-failure larger patient cohorts are needed.

P80 IMPACT OF DONOR HYPERNATREMIA ON OUTCOME AFTER CARDIAC TRANSPLANTATION

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Introduction and Background: Donor hypernatremia is known to be associated with impaired outcome following liver and renal transplantation whereas its impact on outcome after heart transplantation (htx) is still discussed controversially. The impact of donor sodium levels on early morbidity and 1-year-survival following htx should be investigated.
Methods: Between 2010 and 2017 84 patients underwent htx in our department. With regard to donor sodium levels the patients could retrospectively be divided into three groups: a group with donor sodium below 133 mmol/l (group 1), a group with levels between 133 and 156 mmol/l (gr. 2), and a third group with donor sodium >156 mmol/l (gr. 3).
Results and Conclusions: Htx was performed in 9 patients with donor levels below 133 mmol/l, in 63 patients with donor sodium between 133 and 156 mmol/l, and in 12 patients with levels > 156 mmol/l.

Thirty-day-mortality was 11.1 % in patients of gr. 1, 9.5 % in gr. 2 and 16.7 % in gr. 3.

We did not find significant differences between the groups regarding incidence of rejection, renal failure, or severe infection. Duration of mechanical ventilation, stay on intensive care unit and in hospital was slightly prolonged in groups 1 and 3.

1-year-follow up revealed a comparable morbidity between the groups. Coronary allograft vasculopathy occurred only in 2 patients of group 2. The survival rate was 83.3 % (5/6), 77.4 % (41/53), and 72.7 % (8/11) in groups 1,2, and 3.

We could not detect an impaired early outcome in patients receiving hearts from hypernatremic donors. As the 1-year-follow-up results were also comparable between our groups, we think that cardiac allografts from donors with elevated sodium levels can be transplanted with satisfying results.

P81 CALCINEURIN INHIBITOR WITHDRAWAL AND PRE-OPERATIVELY VENTRICULAR ASSIST DEVICE SUPPORT RESULTS IN DE-NOVO DONOR SPECIFIC ANTIBODIES TRIGGERING CARDIAC ALLOGRAFT VASCULOPATHY

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Existing renal failure (RF) pre-heart transplantation (HTx) is a risk factor for decreased survival post-HTx. RF often aggravates due to the chronic use of calcineurin inhibitors (CNI). Thus, for many years CNI weaning strategies have been made to avoid RF.

Our 31-year-old male patient was supported with continuous flow left ventricular assist device (cfLVAD) for 6 months. Post-HTx, induction therapy with antithymocyte globulin was implemented because of existing impaired renal function to delay the start with tacrolimus (TAC).

The initial clinical course of the patient was uneventful besides persistent RF (cGFR 38 ml/min). Biopsy showed no sign of cellular rejection (CR, 0R) at month 6. Thus, we started to wean off TAC to a CNI-free regimen with everolimus (ERL), MMF and steroids at month 9.

At month 10 the patient presented with signs of heart failure because of decreased systolic LV-function and diastolic dysfunction. Biopsy ruled out cellular rejection but detected a form of diffuse CAV affecting the media. We detected dnDSA and a mild CAV (ISHLT grade 1) in the angiography. Therapy of dnDSA consisted of methylprednisolone pulses and reinitiation of TAC to the existing regimen. Moreover, we treated with plasmapheresis, immunoglobulins and rituximab three times over 3 months, followed by extracorporeal photophoresis as chronic therapy.

Clinical symptoms of heart failure disappeared and heart function was restored at the end of therapy. 11 months later biopsy showed no CR and CAV. Renal function remains reduced but stable (cGFR 54 ml/min) and the patient is back to work.

Our case shows that patients with cfLVAD support pre-HTx are more prone to develop dnDSA post-HTx. In such immunologic risk patients with RF CNI-minimizing rather than CNI-withdrawal strategies should be preferred combined with a close monitoring of dnDSA.

P82 GENDER DIFFERENCES IN HEART TRANSPLANT RECIPIENTS

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Introduction and Background: Differences in symptoms, disease course and treatment of heart failure between women and men are known. Possible gender differences in indications, procedural characteristics and outcome are not well established. We aimed to examine gender aspects in heart transplantation and perioperative outcome.
Methods: In $n = 41{,}830$ first time heart transplant recipients 22.7% were women, We analyzed the prospective international United Network of Organ Sharing (UNOS) database. We followed patients for total mortality and the incidence of adverse events such as graft failure, allograft vasculopathy and malignancies.
Results and Conclusions: At transplant, women were younger than men (median age 52 vs. 55 years, $p < 0.001$) suffered less likely from ischemic cardiomyopathy (7.4% in women vs. 18.7% in men, $p < 0.001$) and were less frequently bridged by mechanical circulatory support (14.5% in women vs. 19.6% in men, $p < 0.001$). Transplant urgency was comparable (status 1A at transplant 23.5% in women vs. 25.5% in men, $p < 0.001$).

Patients were observed for a median of 10 years (maximum follow-up time was 26.3 years). We observed 17,937 deaths during follow-up. Survival post heart transplantation was comparable in women and men (hazard ratio (HR) 0.99, 95% confidence interval [0.95, 1.02], $p = 0.43$). There was a trend for higher graft failure for women (HR 1.08 [0.99, 1.19], $p = 0.084$) and significantly lower allograft vasculopathy (HR 0.86 [0.82, 0.89], $p < 0.001$) and malignancy (HR 0.61 [0.57, 0.65], $p < 0.001$).

Women and men differed in indication and procedural characteristics for heart transplantation. Overall survival after heart transplantation was comparable, but the incidence of adverse events was different for women and men. Whether the knowledge on gender differences in patient characteristics and gender-specific risk prediction can support clinical decisions and improve outcome, needs to be shown.

IMMUNOLOGY

P83 TOLEROGENIC PROPERTIES OF B-CELLS IN SOLID-ORGAN TRANSPLANTATION

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Introduction and Background: Achieving immune tolerance is the ultimate goal in solid-organ transplantation. Despite advanced immunosuppressive regimens, allograft rejection remains a severe problem. Several strategies aim at depleting deleterious alloantibody-producing B cells; however, distinct subsets with immunomodulatory function, termed Bregs, may also be targeted. This subgroup has been ascribed tolerogenic properties mediated by the expression of immunosuppressive mediators, such as interleukin-10 (IL-10), Granzyme B (GrB), inhibitory cell-surface receptors or by the secretion of protective antibodies (in particular IgM).
Methods: The effect of immunosuppressive drugs on regulatory B-cell subsets, including transitional immature B lymphocytes ($CD19^+CD24^{hi}CD38^{hi}$) and GrB-producing B cells, was assessed in renal-transplant patients receiving calcineurin inhibitors (CNI). Furthermore, a complementary literature search on innate-like B cells was conducted, emphasizing the central role of IgM in allograft tolerance.
Results and Conclusions: The number of peripheral circulating $CD19^+CD24^{hi}CD38^{hi}$ and IL-10-producing Bregs was significantly reduced in CNI-treated patients and in healthy volunteers receiving CNI. In contrast, the number of GrB-producing regulatory B cells was not affected by CNI. A low percentage of peripheral blood $CD19^+CD24^{hi}CD38^{hi}$ Bregs in renal-transplant patients correlated with a higher incidence of allograft rejection. A similar association has been reported for transplant patients with low serum IgM levels. IgM may directly exert selective pressure on auto-reactive and donor-reactive B-cell clones, also explaining the high DSA clearance rate in lung transplant patients treated with IgM-enriched IVIGs. In conclusion, immunosuppressive therapies should aim to deplete B cells selectively and to preserve the regulatory B-cell subsets that are important for the maintenance and induction of allograft tolerance.

LIVING DONATION

P85 HOW EVALUATION FOR LIVING KIDNEY DONATION SAVED MY LIFE

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Introduction and Background: In order to ensure eligibility for living kidney donation, donor candidates undergo a thorough medical evaluation. This evaluation process might reveal previously unknown medical conditions, leading to declination of the donor candidate. However, detection of such medical conditions may have a lifesaving impact for kidney donor candidates. We report 10-year data from our living donor transplantation program on donor candidates newly diagnosed with impactful medical conditions during the evaluation process.
Methods: A retrospective analysis of living kidney donor candidates since 2007 at our center was performed. Focus was on newly diagnosed medical conditions requiring immediate attention and their prognostic significance.
Results and Conclusions: Since 2007, 341 potential living kidney donor candidates were evaluated, of which 157 (46%) donated a kidney. 174 candidates (51%) were declined, whereas 10 candidates (4%) are still under evaluation. Interestingly, 48 of the declined candidates (28%) were diagnosed with a medical condition requiring immediate attention. While 29 patients were newly diagnosed with diabetes mellitus, 8 patients were diagnosed with cardiac disease requiring intervention and 7 patients were diagnosed with malignancy. These newly diagnosed malignancies comprised NET of the bowel and abdomen, lymphoma, bronchial carcinoma, MGUS and renal cell carcinomas, which directly underwent curative treatment. The other 4 patients were newly diagnosed with CIBD, active hepatitis B or PSC, respectively.

In conclusion, the evaluation process for living kidney donation allowed for revelation of life changing diagnoses in a relevant proportion of candidates, requiring immediate medical attention in order not to affect life expectancy.

P88 A RARE COMPLICATION AFTER RETROPERITONEOSCOPIC DONOR NEPHRECTOMY

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Introduction and Background: Retroperitoneoscopic nephrectomy is an established method of kidney donation. We present a case of an ipsilateral pneumothorax with cervical and mediastinal emphysema as a rare complication of this procedure.
Methods: A 34-year-old woman underwent a left-sided retroperitoneoscopic nephrectomy There were no abnormalities in the preoperative investigations.

Postoperatively she complained of dyspnea and pain in the operated region. The hemoglobin level remained stable, abdominal ultrasound showed no free fluid collection.

On the third postoperative day, after the removing of the central venous line the patient had a brief loss of consciousness and was transferred to ICU. A CT scan showed a low amount of a fluid with a small pneumothorax on the left side and a mediastinal and cervical emphysema. There were no intracranial abnormalities and no significant lesions in the abdomen. The patient underwent a bronchoscopy which showed no tracheal lesion. The thoracoscopy confirmed the presence of a hemothorax which was evacuated. Two chest tubes were placed and removed. after 72 h. On the 11th postoperative day the patient could be discharged.

In the literature, there are some reports about this complication following retroperitoneoscopic surgery. The most common mechanisms are barotrauma, diaphragmatic injuries or congenital diaphragmatic defects.
Results and Conclusions: Pneumothorax can occur without any diaphragmatic injury. The compliance of the retroperitoneal space is lower than that of the intraperitoneal cavity. Therefore, a sudden increase in pressure may result in the rupture of tissues. Paying attention to overall pressure limits and end tidal CO2-levels as well as adequate muscle relaxation might in some cases prevent the occurrence of that rare complication.

P90 THE INFLUENCE OF LIVING AND DECEASED DONOR KIDNEY TRANSPLANTATION ON GRAFT SURVIVAL: A PROPENSITY SCORE MATCHED ANALYSIS

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Introduction and Background: This study evaluates the influence of living related kidney transplantation ($n = 404$) on graft survival beyond pre-operative differences in comparison to deceased donor ($n = 1549$) kidney transplant in a propensity score matched analysis.
Methods: Via propensity scoring, patients were matched for comparing living related to deceased donor organ transplantation. Different propensity score based matching strategies were deployed due to severe differences between the cohorts. Graft survival was analyzed with multivariable Cox regression and Kaplan Meier analysis.
Results and Conclusions: Before adjustment by propensity score matching, graft survival after living related kidney donation is better as compared to deceased donors in Kaplan Meier analysis ($p < 0.001$; log rank) and multivariable Cox regression ($p = 0.001$; HR = 0.539).

Propensity score matching required adjustment due to vast differences between patient groups. Although CIT (cold ischemic time) and duration of dialysis were part of the score, they could not both be deployed in matching because this returned a small sample size ($n = 2 \times 7$). Thus, the first of two matching strategies included duration of dialysis while discarding CIT from propensity matching. The second strategy excluded both variables.

Deploying the first matching strategy showed that hypertension in donors was the only independent risk factor for graft loss ($p = 0.040$; HR: 2.998) while living related donation was no significant influence on graft survival ($p = 0.389$).

Deploying the second matching strategy showed that female donor gender ($p = 0.028$; HR: 2.727) was a risk factor while recipient IgA nephropathy ($p = 0.040$; HR: 0.221) and living donation ($p = 0.021$; HR: 0.398) were independent protective factors for graft survival.

Kidney transplantation after short duration of dialysis is most beneficial for patients, differences between living related and deceased donor organs fade when transplantation is performed early.

BASIC SCIENCE

P91 FGF1 AND AKT ACTIVATION IN C5AR2 DEFICIENT MICE IS ASSOCIATED WITH PROTECTION FROM ISCHEMIA REPERFUSION INJURY

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Introduction and Background: Ischemia reperfusion injury (IRI) causes rapid complement activation and acute kidney injury (AKI) and contributes to delayed graft function after solid organ transplantation. Severe AKI can progress into renal fibrosis
Methods: Here we studied the distinct functions of complement 5a receptor 1 and 2 (C5aR1; C5aR2) a well-established renal IRI and fibrosis model using C5aR1 and C5aR2 deficient mice in comparison to wild type (WT) mice. IRI was induced by 45 min unilateral renal IRI and longitudinal follow up for 1, 7 and 21 days was done by histology, mRNA analysis and functional magnetic resonance imaging (fMRI). Differential protein abundance and phosphorylation status were assessed with high content antibody microarrays and Western blotting.
Results and Conclusions: C5aR-/- mice developed less IRI-induced inflammation and fibrosis than WT mice. C5aR2-/- showed remarkable renal regeneration after IRI which was even more pronounced than in C5aR1-/- mice. Significant up-regulation of the anti-inflammatory IL-10 mRNA in combination with markedly enhanced tubular proliferation and improved renal perfusion were observed in C5aR2-/- IRI kidneys. *In vivo* lectin staining of the glycocalyx demonstrated increased patency of peritubular capillaries in C5aR2-/- mice. Proteomics revealed enhanced abundance of AKT and increased phosphorylation of fibroblast growth factor (FGF1) in C5aR2 -/- IRI kidneys which was confirmed by Western blotting. C5aR1 and C5aR2 deficient mice are partially protected from renal inflammation after IRI. C5aR2-/- kidneys exhibit better renal regeneration and perfusion than those of C5aR1-/-. This was associated with enhanced expression of anti-inflammatory IL-10, pro-angiogenic FGF1 and the pro-survival factor AKT in C5aR2 deficient animals indicating that C5aR2 inhibition might be a novel therapeutic target to prevent AKI and to overcome delayed graft function.

P93 SILENCING OF MHC CLASS I ON PRIMARY HUMAN HEPATOCYTES AS A NOVEL STRATEGY FOR REDUCTION OF ALLOREACTIVITY – A PRELIMINARY IN-VITRO STUDY

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Introduction and Background: Hepatocyte transplantation (HTx) is of large potential as an additional treatment modality for various liver diseases. However, success of HTx is limited by insufficient engraftment/long-term acceptance of cellular allografts due to immunological rejection. Alternative strategies of immunomodulation thus are of special interest. Primary human hepatocytes (PHH) are known to constitutively express MHC class I, consequently silencing of MHC class I expression could potentially reduce the allogeneic immune responses induced upon transplantation and hence improve the outcome of HTx.
Methods: PHH were isolated using a 2-step-collagenase perfusion technique. Expression of MHC class I was silenced using lentiviral vectors encoding for β2-microglobulin (shβ2 m) specific short hairpin RNA (shRNA). A non-specific shRNA (shNS) was used as control. Thereafter PHH were co-cultured with allogeneic lymphocytes (labeled with PKH-26) in terms of a mixed lymphocyte hepatocyte culture (MLHC). Proliferative responses were detected on day 10 of MLHC via flow-cytometry.
Results and Conclusions: The delivery of shβ2 m into PHH caused a decrease by up to 87% in β2 m transcript levels in comparison to shNS. This induced the downregulation of MHC class I cell surface expression by 70%±12% in comparison to shNS-expressing PHH. Subsequently, proliferative responses against silenced PHH were significantly lower than observed for untreated PHH (mean reduction of 60%). Preliminary in-vitro data thus indicate that silencing of MHC class I on PHH might represent a promising approach for immunomodulation in the transplant setting.

P94 IMMUNOSUPPRESSIVE DRUGS IN HEPATOCYTE TRANSPLANTATION - AN IN VITRO ANALYSIS WITH PRIMARY HUMAN HEPATOCYTES

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Introduction and Background: Hepatocyte transplantation (HCTx) is of great potential for the treatment of various liver diseases. Despite successful animal studies, insufficient engraftment and long-term acceptance of cellular allografts though remain major challenges for clinical application in humans. Aim of this study thus was to analyse different immunosuppressive drugs for their potential suitability in HCTx applying an in vitro model with primary human hepatocytes (PHH).
Methods: PHH were isolated from resected liver specimens and co-cultured with allogenic lymphocytes in terms of a mixed lymphocyte hepatocyte culture (MLHC) to characterize the immune response induced. Proliferative alloresponses were determined by flow-cytometry. MLHC was performed in the absence/presence of Cyclosporin, Everolimus, Belatacept and methylprednisolone. The viability and metabolic competence of cultured PHH was assessed by the following parameters: MTT-assay, DNA content, albumin synthesis, urea production and AST-leakage.
Results and Conclusions: Immune responses towards PHH in vitro effectively could be suppressed by Cyclosporin, Everolimus and Belatacept. In contrast to the other immunosuppressants, the application of Everolimus significantly reduced the viability of PHH in vitro. However, further analyses including the courses of DNA content, album synthesis, urea production and AST-leakage showed no significant differences in between the immunosuppressive drugs applied.

P95 **PERSONAL EXPERIENCES WITH A NEW TRAINING CONCEPT IN ESTABLISHMENT OF ORTHOTOPIC RAT LIVER TRANSPLANTATION**

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Introduction and Background: Rat liver Transplantation (LTx) is important animal model to investigate the mechanisms of liver graft rejection and liver ischemia/reperfusion injury. It has been reported that at least 30 procedures was needed to achieve the first survival. We want to facilitate the learning curve of Kamada technique for rat LTx using new learning concept video-assisted PDCA (**p**lan-**d**o-**c**heck-**a**ct) circle.
Methods: The new concept consists of 3 components: theoretic preparation, stepwise practice and problem analysis. In theoretic preparation we learned the anatomy and procedures of LTx. Then microsuture anastomosis, cuff technique anastomosis and splint technique were practiced stepwise in PDCA circle in rat bodies. Each practice was well planned, video-monitored and photodocumented, both of which were in detail analyzed to identify the problem. The solution was planned and implemented in the next round practice. The whole procedures were thereafter trained using PDCA concept. Histologic results were analyzed. At last, we reviewed existing training concepts and their schedules.
Results and Conclusions: After 10 rounds practice, the microsuture anastomosis was handsewn in 10 min with solving the problems (stomal stenosis, leakage and rupture).

After 15 rounds practice, the cuff anastomosis was finished in 3 min with solving the problems (vessels rupture, cuff torsion, kinking and dislocation).

After 5 rounds practice, the splint anastomosis was performed in 3 min with solving the problems (bile duct rupture, bleeding and retraction).

After 13 rounds practice on liver rats, the first 24 h-survival was achieved with anhepatic time 25 min. Histological examination confirmed the surgical quality.

The new learning concept video-assisted PDCA circle can facilitate the learning curve of rat LTx and to reduce the numbers of training animal significantly.