

## KIDNEY PANCREAS

001

## CLINICAL EXPERIENCES WITH A NOVEL ONCE-DAILY TACROLIMUS (LCPT) IN SINGLE PANCREAS AND COMBINED KIDNEY-PANCREAS TRANSPLANTATION: A SINGLE-CENTER REPORT

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**Background:** We retrospectively analyzed the clinical outcome in one single pancreas and 12 simultaneous pancreas-kidney (SPK) patients who were converted from a Tacrolimus extended-release formulation (ER-Tac) to a novel once-daily Tacrolimus (LCPT) due to subtherapeutic Tacrolimus (Tac) levels and suspected Tac-fast metabolization.

**Methods:** Between July 2017 and January 2019, one single pancreas and 12 SPK recipients did not reach the targeted therapeutic Tac-level of 12–14 ng/mL despite a continuous increase of the ER-Tac-dosage. The mean daily dose of ER-Tac was 16.2 mg = 0.19 mg/kg and the mean Tac-level was 7.6 ng/mL at the day of conversion (mean day 10.8). All patients were identified as Tac-fast-metabolizers per a mean quotient of concentration/dosage of 0.42 (0.32–0.57). LCPT was started with mean 15.8 mg (0.18 mg/kg), reaching the targeted Tac-level after mean 2.5 days. The concomitant immunosuppression consisted of an initial lymphocyte depleting agent, MMF and steroids.

**Results:** All patients are alive and insulin-free. At month 1/3/6/9/12, the mean creatinine (mg/dL) was 1.4/1.4/1.3/1.3/1.0, the mean HbA1c (g%) 5.6/5.6/5.6/5.3/5.6, corresponding with an excellent graft function according to the IglS Score. Three clinically suspected pancreatic graft rejections (increase of serum lipase, amylase) were reversible (all at month 1). All complications (acute cystitis, enteritis, BK-viremia, peripancreatic abscess, herpes, hematoma, pancreatic anastomosis bleeding, seroma, leucopenia, bradycardia) were treated successfully. One patient converted to twice-daily immediate-release Tac at month 2 for recurrent diarrhea but no improvement after conversion occurred.

**Conclusion:** Conversion to LCPT in Tac-fast-metabolizing SPK patients with subtherapeutic Tac-levels (despite of a preceding gradual increase of the ER-Tac-dosage) resulted in a prompt reach of therapeutic Tac-levels and overall convincing clinical outcomes.

002

## ORDER OF PANCREAS-KIDNEY TRANSPLANTATION REVISITED – WHICH ORGAN SHOULD OBTAIN THE POLE POSITION FOR REVASCULARIZATION?

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**Introduction:** The preferred order of revascularization during implantation of pancreas and kidney grafts in SPK transplantation is still under debate and solely dictated by the personal surgeon's choice. The first organ implanted benefits from reduced cold ischemia times whereas the following organ might benefit from remote ischemic preconditioning effects. In addition, a plethora of surgical, rheological and immunological effects might influence both organs differentially depending on the sequence of transplantation.

**Material and Methods:** Clinical data of 102 SPK were analyzed. Graft implantation order was determined based on the reported ischemia times of pancreas and kidney grafts. Pancreas and kidney graft survival rates were evaluated with regard to graft implantation order.

**Results:** In 61 transplantations, the pancreas was implanted first (PF), and in 41 SPKs, the kidney was implanted first (KF). Pancreas graft survival at 3 months after transplantation was significantly higher when the kidney was implanted first (7.1 vs. 23% graft loss for KF vs. PF,  $p = 0.034$ ). Kidney graft survival was similar at 3 months (4.9 vs. 4.8% graft loss for PF vs. KF,  $p = 0.971$ ) and 5 years (16.4% vs. 11.9% graft loss for PF vs. KF,  $p = 0.526$ ) after transplantation. Cox multivariate analysis revealed that graft implantation order, donor BMI, recipient age, recipient BMI, donor cause of death and cold

ischemia of the pancreas had independently significant impact on graft survival. A higher frequency of graft pancreatitis ( $p = 0.04$ ), vascular thrombosis ( $p = 0.03$ ), acute rejection episodes ( $p = 0.034$ ), an elevated CRP peak ( $p = 0.001$ ) and delayed graft function of the kidney ( $p = 0.019$ ) were present in PF group compared to KF group.

**Conclusion:** If cold ischemia time can be kept short, a kidney-first approach for revascularization is safe and beneficial for graft function in SPK.

003

## NK CELLS IN KIDNEY TRANSPLANT RECIPIENTS WITH DONOR-SPECIFIC ANTIBODIES – A SYSTEMATIC IMMUNOHISTOCHEMICAL STUDY

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**Background:** There is increasing evidence for a role of NK cells in antibody-mediated transplant rejection (ABMR) of kidney allografts. However, their abundance and compartment-specific distribution is unclear, since specific markers are missing. One innovative approach may be double staining of CD16 and intracellular Tbet. The objective of the present study was to assess the distribution of NK cells in patients with late ABMR.

**Methods:** This study included 86 DSA+ patients with protocol biopsies (BORTEJECT trial, NCT01873157). Rejection features were classified following Banff 2013 and 83 biopsies were analyzed by MMDx™. Using immunohistochemistry, biopsies were double stained for CD16 and Tbet as well as CD34 to enable intracapillary detection of NK cells.

**Results:** Fifty subjects were categorized as ABMR+ and 36 were ABMR-. NK cells were identified in glomeruli and PTC, with a median of 51.8 (IQR: 23.7–131.8) cells per mm<sup>2</sup> cortex (glomeruli) and 10.3 (IQR: 3.4–27.5) cells per mm<sup>2</sup> cortex (PTC). There was a highly significant ( $p < 0.0001$ ) difference in cell counts between ABMR+ and ABMR- patients [glomeruli: 103.4 (46.8–181.1), PTC: 23.8 (10.5–33.8) vs. glomeruli: 36.4 (17.5–50.0), PTC 3.2 (1.5–6.0);  $p < 0.0001$ ]. NK cell counts tightly correlated with the molecular ABMR score (PTC:  $\rho = 0.731$ ,  $p < 0.0001$ ; glomeruli:  $\rho = 0.596$ ,  $p < 0.0001$ ). We found tight correlations between the morphologic findings of peritubular capillaritis and glomerulitis with NK cell number in PTC ( $\rho = 0.69$ ,  $p < 0.0001$ ) and glomeruli ( $\rho = 0.51$ ,  $p < 0.0001$ ). However, NK cell counts were less strongly associated with transplant glomerulopathy ( $\rho = 0.365$ ,  $p = 0.001$ ). We found no significant impact of NK cell counts (< or > median NK cell count in PTC or glomeruli) on transplant survival rates.

**Conclusions:** Our data support the frequent finding of NK cells in two major compartments – PTC and glomeruli. NK cell counts may correlate with the diagnosis of ABMR and molecular features, but in our preliminary analysis had no effect on graft survival.

004

## THE IMMUNE REGULATION COHORT STUDY – A PROSPECTIVE STUDY EVALUATING LYMPHOCYTE SUBPOPULATION KINETICS IN RENAL ALLOGRAFT RECIPIENTS WITH AND WITHOUT REJECTION

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**Background:** Rejection, a leading cause of renal allograft (KTx) loss, crucially depends on lymphocyte-mediated immune responses. Our primary aim was to study differences in immune cell subpopulation between rejecting and non-rejecting KTx.

**Methods:** Recipients of a first KTx without prior maintenance immunosuppression were included. Lymphocyte subsets were measured immediately prior to KTx, as well as at 1, 8, and 52 weeks thereafter. B- and T-cell subpopulations were evaluated using a highly standardized cell isolation and flow cytometry protocol developed in cooperation with Becton Dickinson (panels 1: Tregs; Panel 2: Treg subsets and Tef; 3: CD39<sup>+</sup> Treg, CD8<sup>+</sup> Treg, and Tr-1 cells; 4: B-cell subsets; 5: alternate Treg subsets).

**Results:** Seventy-four KTx recipients (male/female: 50 (67.6%)/24 (32.4%); age  $55.1 \pm 11.84$  years; preemptive/HD/PD 2 (2.7%)/60 (81.1%)/12 (16.2%); dialysis vintage:  $34.6 \pm 19.6$  months; donor age  $58.1 \pm 15.1$  years; HLA-MM  $3.6 \pm 1.21$ ) were included. After a mean of  $44 \pm 74.3$  days, thirteen patients (17.6%) experienced biopsy-proven rejection during follow-up (TCMR: borderline 2 [16.7%]; BANFF 1B: 3 [25%]; 2A: 5 [41.7%]; 2B: 1 [8.3%]; 3: 1 [8.3%]; AMR: 3 episodes).

There was no significant difference in age, dialysis vintage, number of HLA mismatches, or donor age between rejecting and non-rejecting patients. Preliminary data show that at baseline, prior to KTx, rejecting patients had significantly higher relative frequencies of CD3<sup>+</sup>CD4<sup>+</sup> T cells ( $48.5 \pm 10.39$  vs.  $42.8 \pm 8.82\%$  of lymphocytes;  $p = 0.042$ ) compared to non-rejecting patients. At baseline, there were no significant differences in any other studied lymphocyte subpopulation.

**Conclusions:** These preliminary data show that prior to KTx, rejecting and non-rejecting patients show similar lymphocyte subpopulations. Follow-up data after KTx will show whether lymphocyte subpopulations differ during follow-up, and whether they may be of clinical use in diagnosing rejection.

005

### PROTEOMICS REVEALS MOLECULAR WINDOW AND METABOLISM OF NORMOTHERMICALLY PERFUSED HUMAN KIDNEYS

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**Background:** Proteomic profiling by mass spectrometry (MS) can rapidly identify significant changes to proteins. The purpose of applying proteomics to tissue samples was to determine differences between normothermically perfused discarded human kidneys with and without urine recirculation (URC).

**Methods:** Biopsies from 19 NMP kidneys were prepared for proteomics. Protein was extracted from 16 kidneys with URC and from 3 kidneys without. For each kidney analysed with URC ( $n = 8$  DBD and  $n = 8$  DCD kidneys, at least 12 h of NMP), the zero biopsy and tissue taken after 6, 12 or 24 h underwent protein extraction. The proteins were identified and quantified by MS. Quantitative MS data were uploaded to Perseus for data visualization and statistical analysis.

**Results:** Damage-associated molecular patterns (DAMPs) known to be contributing to ischemia reperfusion injury (IRI) were significantly downregulated in kidney tissue after 6 h of NMP with URC compared to kidneys without. Mitochondrial succinate dehydrogenase proteins were significantly downregulated with URC. The protein for the gene angiotensinogen (AGT) was upregulated in kidneys without URC and downregulated in kidneys with URC. The protein for carbonic anhydrase (CA1), maintaining acid-base balance, was upregulated in kidneys with URC and downregulated without. Key enzymes involved in glucose metabolism, including mitochondrial MDH and GOT, were downregulated in DCD zero biopsies compared to DBD. After 12 and 24 h of NMP, enzymes involved in glucose metabolism were more upregulated in DCD tissue compared to DBD. The cytosolic and the mitochondrial phosphoenolpyruvate carboxykinase (PCK) were more upregulated after 24 h of NMP in DCD compared to DBD tissue.

**Conclusion:** NMP with URC is an optimal and feasible preservation method to minimize IRI in discarded human kidneys. Kidneys become metabolically active during NMP. DCD organs seem to benefit more from NMP with/without URC, showing more active glucose metabolism.

006

### EARLY POSTOPERATIVE BASAL INSULIN THERAPY FOR THE PREVENTION OF DIABETES MELLITUS ONSET AFTER KIDNEY TRANSPLANTATION: AN OPEN-LABEL, MULTICENTRE, RANDOMISED CONTROLLED, CLINICAL TRIAL

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**Background:** Immediate postoperative hyperglycemia in kidney transplant recipients (KTRs) associates with overt posttransplantation diabetes mellitus (PTDM) and mortality. We examined efficacy and safety of basal insulin therapy, hypothesizing that PTDM-incidence could be reduced by pancreatic  $\beta$ -cell protection.

**Methods:** Our trial (NCT03507829) followed the previous "TIP-study" (PMID22343119) design. We randomized KTRs without previous diabetes into a treatment group, for immediate postoperative capillary glucose monitoring 4x daily versus a standard-of-care control group, for routine fasting whole-blood glucose. Treatment-group-KTRs were foreseen to receive intermediate-acting insulin-isophane after their first evening glucose surpassed 140 mg/dL. Control-KTRs were foreseen to receive short-acting insulin (sliding scale) for fasting glucose  $\geq 200$  mg/dL, and subsequently antidiabetics, if necessary. Primary endpoint was 12-months PTDM-incidence (derived from oral glucose tolerance tests and treatment necessity). Secondary endpoints included hypoglycemic events, 24-months PTDM-incidence, HbA1c-levels and the relationship between protocol-adherence and PTDM.

**Results:** Of  $N = 263$  participants ( $N = 133$  [treatment];  $N = 130$  [control]),  $N = 216$  ( $N = 105$  [treatment];  $N = 111$  [control]) completed 12-months and  $N = 202$  ( $N = 100$  [treatment];  $N = 102$  [control]) 24-months follow-up. Polycystic kidney disease and diabetes family history were 2.2-fold, respectively, 1.8-fold among treatment-KTRs, despite randomization. HbA1c was significantly lower at 3 months ( $5.7 \pm 0.9\%$  [treatment] versus  $5.4 \pm 0.5\%$  [control],  $p = 0.001$ ) but similar at 6, 12 and 24 months. Twelve-month and 24-month PTDM-incidence among treatment- versus control-KTRs was 10% versus 15%, and 10% versus 16%, respectively (adjusted odds ratios [95% confidence intervals] = 0.41 [0.15–1.06], = 0.38 [0.13–1.09], respectively). Twelve-month and 24-month permanent antidiabetics requirement among treatment- versus control-KTRs was 5% versus 11%, and 2% versus 9%, respectively (adjusted ORs [95% CIs] = 0.34 [0.11–1.09], = 0.16 [0.03–0.87], respectively). Hypoglycemic events among treatment- versus control-KTRs were 11% versus 2% ( $p = 0.006$ ). Delay of postoperative insulinization ( $>2$  days) after first glucose  $\geq 140$  mg/dL, and missing glucose measurements among treatment-KTRs were significantly associated with 12- and 24-month PTDM-incidence.

**Conclusions:** Treatment was safe, the primary endpoint negative, but markedly fewer treatment- than control-KTRs required antidiabetics through follow-up. PTDM-incidence was low in both groups. Excellent treatment protocol-adherence associated with reduced PTDM-incidence.

## LUNG HEART

007

### TACROLIMUS CONCENTRATION-TO-DOSE RATIOS IN HEART TRANSPLANT RECIPIENTS AND RELATIONSHIP TO CLINICAL OUTCOMES

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**Background:** Tacrolimus (Tac) is a part of the standard immunosuppressive regimen after heart transplantation (HTX). However, its metabolism rate is highly variable. Low Tac concentration-to-dose ratios (CDRs), or rapid metabolizers (RMs), have been associated with poor graft function outcomes and higher acute rejection (AR) rates in renal transplantation. We explored rate of RM and differences in outcomes between patients with low Tac CDRs and high Tac CDRs (ie, non-rapid metabolizers [NRMs]) in a HTX patient population.

**Methods:** Between 2002 and 2018, a total of 150 patients were included. At the first out-patient visit all patients will be analysed for their CDR. CDR will be defined by the Tac blood trough concentration (C) divided by the daily dose (D). Patients with a Tac C/D ratio  $< 1.05$  ng/mL  $\times$  1/mg will be characterized as RM and those with a C/D ratio  $\geq 1.05$  ng/mL  $\times$  1/mg as NRM. Further DCR analyses will be made at 3, 6, 9 and 12 months. Change in CDR will be analysed over time. Patients who will change groups from RM to NRM or the other will be analysed as a subgroup. Primary endpoint will be a composite endpoint consisting of death or acute rejection (treated or biopsy proven). Secondary endpoints will be: severe infection and drug-related side effects (tremor, polyneuropathy, new onset of diabetes).

**Results:** Results will be shown at the meeting.

**Conclusion:** Calculation of the Tac C/D ratio 1–3 months after HTX may assist physicians in their daily clinical routine to identify Tac-treated patients at risk for the development of acute rejections, side effects or even higher mortality.

008

### TEMPORARY STOPPING OF IMMUNOSUPPRESSION IN HEART TRANSPLANTED PATIENTS WITH SEPSIS

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**Background:** Permanent immunosuppression in heart transplant patients is associated with a higher risk for infections, which, in some cases, can

aggravate into life threatening septic complications. A potential option to save these patients is to temporarily decrease or stop immunosuppression. Until now, no data exist, if it is possible in heart transplant patients. The aim of this study is to investigate the influence of temporary stopping immunosuppressive therapy (SIS) in patients after heart transplantation on defined outcomes using a retrospective analysis.

**Methods:** The study population comprised 25 patients (88% male), transplanted between 2006 and 2015. Included were those patients who developed sepsis within the first 3 months after HTX and whose immunosuppressive therapy was temporarily paused. Exclusion criteria were patients <18 years and all patients not treated in the cardiac surgical intensive care unit at our hospital. Kaplan–Meier analysis was used to calculate survival. The Mann–Whitney *U*-test was used to test the difference in the time to pause immunosuppression between survivors and non-survivors.

**Results:** The average patient age at the time of transplantation was  $58.9 \pm 11.5$  years. All patients had a triple immunosuppressive therapy, with cyclosporine A or tacrolimus together with mycophenolate mofetil and steroids. An overall incidence SIS was detected in 8.0% of all 377 cases. The comparison of the temporary stopping of therapy with a median duration for survivors of 5 days and for deceased of 8 days, did not show a significant difference ( $p = 0.397$ ). While stopping SIS was initiated at a median of 19 days post-transplant in surviving patients, deceased patients had a later median stop of IS (31 days). The difference with a small to moderate standardized effect size  $r$  was 0.26, however, did not reach a significant level ( $p = 0.216$ ). The analysis results for primary endpoint evaluation showed the highest mortality rate, with 50% of the patient population dying within the first 4 months after HTX. The survival rate at 90 days (3 months) was 52%, at 1 year 44% and at 5 years 24%. Overall, rejections occurred in three patients (12.5%) with an average of 4.5 days after the re-start of immunosuppressive therapy.

**Conclusions:** Temporary pausing of immunosuppression in patients with severe septic complications seems to be safe and not associated with a higher rate of rejection. However, patients are still prone to a higher risk of death, especially if the sepsis developed in the early phase after heart transplantation.

#### 009 PEDIATRIC HEART TRANSPLANTATION IN HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY – A CASE SERIES

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**Background:** Hypertrophic obstructive cardiomyopathy (HOCM) remains an important entity in the field of pediatric cardiomyopathies, being associated with a remarkable risk of sudden cardiac death. Here we present a case series of five children undergoing heart transplantation due to HOCM.

**Methods:** Within the last decade, five children (mean age 15 years) underwent heart transplantation (HTX) at our institution. Patient history, genetic screening as well as outcome after HTX was evaluated.

**Results:** Age of diagnosis varied from 2 months to 15 years. One patient was diagnosed HOCM in the setting of cardiopulmonary resuscitation and was bridged to transplant on veno-arterial extracorporeal membrane oxygenation. Three patients underwent implantation of a defibrillator for primary prophylaxis and received adequate shock therapy during waiting period. Family screening revealed positive family history in three patients, genetic counselling showed MYBPC3 mutation in two patients and MYH7 mutation in one patient. Median waiting time to HTX was 48 days (range 11–642 days). All patients received excellent organs (median age 18 years, median ischemic time 180 min) and recovered from HTX uneventfully. During a mean follow up period of 38 months one patient suffered from post-transplant lymphoma, while four patients report optimal quality of life.

**Conclusions:** Patients with a genetic background were diagnosed within 3 years after birth and suffered from a more aggressive course of the disease. Heart transplantation was associated with excellent postoperative outcome, long-term survival remains challenging due to the young age of this patient cohort.

#### 010 BODY COMPOSITION QUANTIFIED BY PRE-TRANSPLANTATION COMPUTED TOMOGRAPHY SCANS PREDICTS A WORSE OUTCOME AFTER DOUBLE-LUNG TRANSPLANTATION IN ELDERLY RECIPIENTS

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**Background:** Especially in elderly lung transplant (LuTx) candidates, pre-transplant frailty and body composition are increasingly recognized as risk

factors for a worse post-transplant outcome. Here, we aimed to assess the clinical outcome after LuTx in elderly patients who were stratified by body composition based on pre-transplant chest CT scans.

**Methods:** We retrospectively included patients  $\geq 60$  years who received LuTx at the Medical University of Vienna from December 1998 to December 2018, and who had available pre-transplant (not older than 1 year) CT scans. The mediastinal fat areas at the level of the carina, as well as the dorsal muscle group (DMG) areas at the level of the 12th thoracic vertebral body, were calculated semi-automatically using OsiriX (Pixmeo, Switzerland). The adjusted and normalized data were correlated with clinical parameters.

**Results:** There were 114 patients included in the analysis, of which 86 (75.4%) were male and 28 (24.6%) were female. The mean age at transplantation was  $63 \pm 2.7$  years. The two most frequent diagnoses were COPD (50.9%) and fibrosis (40.4%). Patients were assigned to three groups according to body composition (“high risk”: low muscle mass and high mediastinal fat ( $n = 12$ ); “low risk”: high muscle mass and low mediastinal fat ( $n = 8$ ); and “intermediate”: any other ( $n = 94$ )). The time of ventilation ( $p = 0.022$ : 480 vs. 43 h), the stay in the ICU ( $p = 0.001$ : 38 vs. 5 h), and the stay in hospital ( $p = 0.001$ ; 66 vs. 19 days) were significantly longer in the “high-risk” group compared to the “low-risk” group. “High-risk” group patients compared to “low-risk” group patients had a significantly increased risk for wound infections ( $p = 0.001$ ), delirium ( $p = 0.042$ ), and tracheostomy ( $p = 0.017$ ).

**Conclusion:** The assessment of morphometric parameters using chest CT scans in LuTx candidates is a promising, objective, and easily applicable tool with which to identify patients with diminished outcomes after LuTx. Moreover, this assessment emphasized the crucial importance of physical activity and rehabilitation measures in LuTx.

#### 011 LUNG TRANSPLANTATION FOR PULMONARY HYPERTENSION WITH GIANT PULMONARY ARTERY ANEURYSM

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**Background:** Aneurysm of the main pulmonary trunk (PAA) is a rare but severe complicating factor in patients suffering from pulmonary arterial hypertension (PAH). Many centers consider a PAA as an indication for a heart-lung transplantation. We, herein, aimed to summarize our institutional experience with a lung-only strategy in this complex group of patients.

**Methods:** We performed a retrospective single-center analysis of PAH patients with a severe PAA receiving lung transplantation between 01/1996 and 11/2018.

**Results:** A total of 128 PAH patients were transplanted within the study period. Eight patients presented with a severe aneurysm of the pulmonary trunk (mean diameter: 72.6 mm). Donor lungs were procured together with the main PA. In the recipient, cardiopulmonary bypass with bicaval cannulation was established and bilateral pneumonectomy together with resection of the entire PA trunk was performed. The right donor lung was implanted and the attached PA trunk was pulled through behind the SVC and ascending aorta. Anastomosis was performed just above the level of the pulmonary valve. Thereafter, the left lung was implanted by re-connecting the left PA to the main PA trunk. All but one patient, who died from sepsis on POD13, were successfully discharged. Long-term survival was good and did not differ from outcome of non-aneurysmatic PAH patients (log-rank:  $p = 0.461$ ).

**Conclusion:** This is, to the best of our knowledge, the largest published expertise of PAH patients transplanted with a PAA. We could show that these patients are eligible for double lung transplantation and do not require a heart-lung transplantation.

#### 012 UPDATE OF THE INNSBRUCK LUNG TRANSPLANTATION PROGRAM: DEMOGRAPHICS AND OUTCOMES OF 25 YEARS

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**Background:** After the first pioneering attempts in lung transplantation in the eighties, the program was re-established in 1993 and has been playing a continuous role in patient care of western Austria ever since.

**Methods:** Survival and demographic data were analysed. All lung transplantations from November 1993 to May 2018 were included. Data were collected and analysed retrospectively. Continuous variables are provided as medians and categorical variables are displayed in absolute numbers and/or percentages. For survival analysis the Kaplan–Meier method was used.



**Results:** Altogether, 274 lung transplantations were performed in 142 men (51.8%) and 132 women (48.2%). Median age was 55 years. An increase in median recipient-age is significant with 53.5 years (nineties), 54 years (noughties) and 57 years (2010s),  $p = 0.019$ . The underlying conditions were chronic obstructive pulmonary disease (63.1%), idiopathic pulmonary fibrosis (9.9%), alpha 1-antitrypsin deficiency (6.6%), cystic fibrosis (6.6%) as well as other diseases (13.9%). In the majority (81.8%) a bilateral transplantation was performed. In two patients additional heart valve surgery was done. Overall median survival was 78 and 85 months for bilateral transplant recipients, respectively. Significant increase of 10-year-survival was reached comparing the nineties (25%) and the noughties (36%),  $p = 0.003$ . For the 2010s, 10-year-survival data are not yet available but the trend is very promising. Major causes of death are still rejection with or without development of bronchiolitis obliterans, infectious diseases especially pneumonia based on CMV reactivation and malignant diseases.

**Conclusions:** The results are comparable with international registries. Recipient age is increasing as well as post-transplant survival.

## YOUNG INVESTIGATOR AWARDS

013

### TUBULAR ECTASIA IN RENAL ALLOGRAFT BIOPSY: ASSOCIATIONS WITH OCCULT OBSTRUCTIVE UROLOGICAL COMPLICATIONS

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**Background:** Urological obstructive complications (UOC) occur in up to 15% of kidney transplants (KTX). Most cases are excluded by ultrasonography (US); however in the early post-transplant phase, accuracy may be limited as in the case of delayed graft function (DGF) and reduced urinary output high-grade hydronephrosis may not be observed. Features of acute tubular injury (ATI) in KTX biopsy may be informative but existing literature is scarce with respect to a distinct histological phenotype indicating UOC. In experimental data, tubular ectasia (TE) was shown to be associated with UOC. We evaluated the association of histomorphological features, particularly TE, with occult (= without relevant hydronephrosis in US) UOC and renal outcomes.

**Methods:** We included 976 of 1537 consecutive KTX recipients who had an early indication biopsy. The biopsy finding of TE classified as "suspicious of UOC" was compared with clinical outcomes: DGF, estimated glomerular filtration rate, and occult UOC. Additionally, a single pathologist blinded to the clinical results reevaluated all the biopsies with regard to quantification of TE and investigating further distinct features of ATI.

**Results:** Fifty-eight (5.9%) patients presented with TE, which was not related to DGF or eGFR. Forty percent of patients had a UOC (mostly ureteral stenosis). Comparing these biopsies to matched controls, TE was significantly associated with UOC (odds ratio 2.69;  $p = 0.018$ ). After histopathological reevaluation including TE and other features of ATI, we developed a final multivariate model with a highly significant relationship to UOC (Receiver operating characteristic-area under the curve: 0.77;  $p = 0.001$ ). The model provides a specificity of 78% and negative predictive value of 73%.

**Conclusions:** TE together with additional signs of ATI is indicative of occult UOC. This histological phenotype should prompt more detailed evaluation for UOC when there is no evidence of relevant hydronephrosis in the ultrasonography.

014

### A CASE-CONTROL MATCHED COMPARISON OF KIDNEY TRANSPLANTATION FOLLOWING CONTINUOUS HYPOTHERMIC MACHINE PERFUSION VS. STATIC COLD STORAGE

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**Background:** Improved kidney preservation remains an unresolved issue in kidney transplantation. The aim of this study was to assess the effect of hypothermic machine perfusion (HMP) vs. static cold storage (SCS) in kidney transplantation.

**Methods:** All kidney transplantations performed at the Medical University of Innsbruck between August 2015 and December 2018 ( $n = 422$ ) were evaluated. HMP was applied in 105 kidneys, and the remaining 317 kidneys were transplanted following SCS. The comparison was performed employing case-control matching. The assessment eventually included 210 patients (105 HMP, 105 CS) fitting the criteria. DGF was defined as  $>1$  hemodialysis.

**Results:** Mean CIT in HMP and CS kidneys was 17:01 and 13:35 h, respectively. Patient survival after a median follow-up of 20 months (range 1–41 months) was 97.2% (CS: 95.7% vs. HMP: 98.8%;  $p = 0.796$ ). Graft survival was 89.1% in CS kidneys and 96.5% in the HMP organs ( $p = n.s.$ ). Delayed graft function (DGF) occurred in 38.8% and was less frequent in SCD donors compared to ECD organs (15.3% vs. 23.4%;  $p = 0.010$ ). DGF occurred less frequently after HMP compared to CS (15.8% vs. 23.0%;  $p = 0.029$ ). There was a tendency towards less frequent DGF in ECD organs transplanted following HMP compared to CS (10.5% vs. 12.9%). This was even more pronounced in SCD (5.3% following HMP compared to 10.0% after CS,  $p = 0.034$ ).

**Conclusion:** Our results indicate that HMP is beneficial not only for ECD kidneys but also for SCD kidneys. HMP should be used as desirable method of preservation.

015

### THE IMMUNE REGULATION COHORT STUDY – ALTERATIONS IN LYMPHOCYTE SUBPOPULATIONS IN TRANSPLANT-LISTED DIALYSIS PATIENTS COMPARED TO HEALTHY CONTROLS

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**Background:** Uremia increases morbidity and mortality. Previous studies indicated that dialysis patients show significant quantitative and qualitative alterations in lymphocyte populations compared to healthy controls. However, there is only very limited data on many T- and B-cell subsets. The aim of this study was to provide a detailed understanding of the extent of lymphocyte alterations in dialysis patients.

**Methods:** Kidney transplant (KTx) listed CKD 5D patients without prior maintenance immunosuppression and healthy controls were included. B- and T-cell subpopulations were evaluated using a highly standardized cell isolation and flow cytometry protocol developed in cooperation with Becton Dickinson (panels 1: regulatory T cells (Tregs); Panel 2: Treg subsets and Tef; 3: CD39<sup>+</sup> Treg, CD8<sup>+</sup> Treg, and Tr-1 cells; 4: B-cell subsets; 5: alternate Treg subsets).

**Results:** Seventy-four KTx recipients (male/female: 50 [67.6%]/24 [32.4%]; age 55.1  $\pm$  11.84 years; dialysis vintage: 34.6  $\pm$  19.59 months) and 74 healthy controls (male/female: 23 [31.1%]/51 [68.9%]; age 46.0  $\pm$  15.88 years) were included.

Kidney transplant candidates showed significant alterations in lymphocyte subpopulations compared to healthy controls: While the relative frequency of CD3<sup>+</sup>CD4<sup>+</sup> T cells and CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup>Tregs among lymphocytes was not different, there were significantly more CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>hi</sup> (5.6 [5.2–6.4] vs. 4.3 [3.8–4.7];  $p < 0.001$ ) and CD4<sup>+</sup>CD25<sup>+</sup>CD127<sup>dim</sup> (7.0 [6.8–8.0] vs. 5.7 [5.3–6.5]%) of CD3<sup>+</sup>CD4<sup>+</sup>;  $p < 0.001$ ) Tregs in dialysis patients compared to healthy controls. Within CD4<sup>+</sup>CD25<sup>+</sup>CD127<sup>dim</sup> Tregs, there was no difference in effector and proliferating effector Tregs, while significantly less naive Tregs (29.3 [27.6–33.4] vs. 35.0 [31.7–37.8]%;  $p < 0.001$ ) were found in transplant candidates compared to controls.

**Conclusions:** This study provides a detailed analysis of lymphocyte subpopulation alterations in uremia compared to normal renal function. Preliminary data suggest a profound change in the relative frequency of Treg subpopulations. The follow-up of this study will enable an assessment as to whether these changes are reversible with established graft function and whether they are associated with graft rejection.

016

### COMPARISON OF DONOR SCORING SYSTEMS IN PREDICTING OUTCOME AFTER LUNG TRANSPLANTATION – A RETROSPECTIVE DATA ANALYSIS

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**Background:** Donor evaluation and adequate judgement of organ offer suitability are fundamental for recipient results in lung transplantation. The prediction of post-transplant outcomes has been the proposed aim of several donor scoring systems; however, none of them have yet gained widespread use in lung transplantation. The aim of this study was to compare four different donor scoring systems (Oto, ET, ODSS and MALT) and their correlation with early- and long-term outcomes.

**Methods:** This retrospective study included all patients who received standard double lung transplantation between January 2010 and December 2018 at the Division of Thoracic Surgery at the Medical University Vienna. Four scores were calculated for each patient: Oto and colleagues proposed a scoring system incorporating five donor factors (age, smoking history, chest X-ray, secretions in bronchoscopy and  $\text{paO}_2/\text{FiO}_2$  ratio). The ET score incorporates donor history parameters along with the variables of the Oto score. The ODSS score includes the donor factors diabetes mellitus and race in addition to donor age and smoking status. The MALT score, in contrast, is the only one to also include recipient characteristics. Early- and long-term outcomes based on these four scores were compared.

**Results:** Length of mechanical ventilation could not be predicted by the Oto score ( $p = 0.116$ ) but was significant for the ET score ( $p = 0.002$ ), ODSS score ( $p = 0.026$ ) and MALT score ( $p < 0.001$ ). Time in the intensive care unit was prolonged in high-risk ODSS score ( $p = 0.047$ ) patients and high-risk MALT score ( $p < 0.001$ ) patients compared to intermediate- and low-risk patients. The MALT score was the only significant predictor for total hospitalization time ( $p < 0.001$ ) and for PGD 3 rates at all time points ( $t_0$ :  $p < 0.001$ ,  $t_{24}$ :  $p = 0.011$ ,  $t_{48}$ :  $p = 0.003$ ,  $t_{72}$ :  $p = 0.027$ ). The ODSS score did show a trend towards improved prediction for length of hospitalization ( $p = 0.055$ ). Graft survival was significant for the Oto score ( $p = 0.001$ ), ODSS score ( $p = 0.001$ ) and MALT score ( $p < 0.001$ ), while the ET score could not predict long-term survival ( $p = 0.053$ ).

**Conclusion:** Overall, the MALT score appeared superior in predicting relevant postoperative outcomes in lung transplantation when compared to the Oto, ET and ODSS score. This underlines the importance of both donor and recipient variables for improving prognosing post-transplant results.

### 017 DEVELOPMENT OF MHC-SPECIFIC IGE IN A MURINE MODEL OF ACUTE ANTIBODY-MEDIATED REJECTION

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**Background:** Transplantation is the gold standard for treatment of patients with end-stage organ failure. While the 1-year graft survival rate has increased significantly by standard immunosuppression, long-term allograft survival is still limited due to antibody-mediated rejection (ABMR) caused by either pre-existing or de novo donor specific antibodies (DSA). The occurrence of DSA of the IgG isotype is strongly correlated with an increased risk of graft loss and screening of HLA-specific DSA of the IgG isotype is included in standard procedures of clinical transplantation. To our knowledge, our group was the first to describe anti-MHC DSA of the IgE isotype in mice and humans upon allograft rejection. IgE is mainly associated with Th2-type immune responses, such as type I allergy, and parasite infections.

**Methods:** For further studies on the role of MHC-specific IgE in humoral rejection, we transplanted fully mismatched BALB/c skin allografts onto CCR5KO recipients, which is a model of acute ABMR, and performed re-transplantation of donor skin 3 weeks thereafter. The development of alloreactive IgG antibodies was assessed via flow cytometry. For measurements of MHC-specific IgE and IgG1 we used a custom-made ELISA employing MHC class I and II monomers, which allows us to distinguish between MHC class I and class II DSAs.

**Results:** Although allograft survival in CCR5KO mice was not significantly different compared to wild type C57BL/6 mice, the production of DSAs occurred much earlier and IgG DSA levels measured via flow cytometry were significantly higher. Using our MHC-specific ELISA, we were able to demonstrate the production of MHC-specific IgE upon acute humoral rejection. Furthermore, we also show that MHC-specific IgE levels increase after re-transplantation similar as it was observed for MHC-specific IgG.

**Conclusion:** We could show that MHC-specific IgE is present upon allograft rejection in a murine model of acute ABMR and that donor-specific IgE levels were increased after re-transplantation similar to what is known for IgG.

### 018 EXTENSIVE PHENOTYPIC IMMUNE MONITORING IN A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF PROPHYLACTIC USE OF EXTRACORPOREAL PHOTOPHERESIS (ECP) IN DE NOVO LUNG TRANSPLANT RECIPIENTS

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**Background:** Extracorporeal photopheresis (ECP) is a therapeutic option for the treatment of acute and chronic rejection after solid organ transplantation. In

a randomized controlled trial that investigates the addition of prophylactic use of ECP to a tacrolimus-based immunosuppressive regimen after lung transplantation, a comprehensive phenotypic immune monitoring is performed to assess the immunomodulatory effects of ECP.

**Methods:** To date, 35 (from calculated sample size of 62) end-stage chronic obstructive pulmonary disease (COPD) patients received bilateral lung transplantation and were randomized into 2 treatment arms: standard triple immunosuppression with or without ECP. For each patient of the ECP group, a total of 16 ECP treatments are performed over a period of 13 weeks. For monitoring leukocyte subsets such as regulatory T cells (CD4+CD25+FoxP3+ Tregs) and regulatory B cells (CD19+CD5-CD1d+ Bregs), polychromatic flow cytometry analysis is performed on fresh whole blood samples using validated, standardized, lyophilized monoclonal antibody panels (DuraClone). Sample acquisition took place before and 3 months after transplantation, when the last ECP treatment was conducted, as well as 6 months after transplantation.

**Results:** From 35 bilateral lung transplanted patients, 20 patients have reached their 3-month visit and 14 patients their 6-month visit, which are analyzed here. No significant difference in the frequency of Tregs or Bregs between both groups was found at baseline (Tregs  $p = 0.106$ ; Bregs  $p = 0.407$ ). At 3 months, Tregs have significantly decreased in the non-treated population ( $p = 0.001$ ) while in the ECP-treated group no significant decline was seen ( $p = 0.176$ ). Regarding Bregs no significant difference was found but a trend towards a post-transplant increase in both groups was noted (non-treated  $p = 0.075$ ; treated  $p = 0.058$ ).

**Conclusions:** Preliminary data from an interim analysis of double lung transplanted patients receiving ECP as prophylactic treatment suggest that ECP prevents the post-transplant decline in Treg frequency seen with standard immunosuppression.

### 019 DIFFERENTIAL ROLE OF MAJOR AND MINOR ANTIGEN DISPARITIES FOR TOLERANCE INDUCTION AND MAINTENANCE

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**Background:** Transplantation tolerance through mixed chimerism constitutes a promising strategy to avoid the undesired side effects of immunosuppressive medication and to prolong allograft survival. Nevertheless, its implementation as a clinical routine remains controversial due to the cytoreductive conditioning required for bone marrow (BM) engraftment. Recently, we found that transiently depleting natural killer (NK) cells at the time of transplantation can obviate the need for irradiation when conventional doses of fully mismatched BM are transplanted into non-irradiated mice under costimulation blockade and rapamycin. Despite persistent levels of mixed chimerism, BMT recipients gradually rejected skin grafts from the same donor. To elucidate the lack of tolerance in stable mixed chimeras, we depleted NK cells permanently and challenged recipients with distinct donors exhibiting varying degrees of major and minor antigen disparities.

**Methods:** C57BL/6 ( $\text{H2}^b$ ) mice received costimulation blockade ( $\alpha$ -CD40L and CTLA4-Ig), a short course of rapamycin and  $20 \times 10^6$  unseparated BM cells from different donors. Selected donors either displayed only minor antigen (miHA) mismatches (BALB.B,  $\text{H2}^b$ ), only major antigen (MHC) mismatches (B10.D2,  $\text{H2}^d$ ) or both (BALB/c,  $\text{H2}^d$ ). To exclude NK cell alloreactivity we deployed two types of F1 donors ( $\text{H2}^{b/d}$ ), one with a mixed B6/BALB/c minor antigen background (CB6F1) and one with BALB/c minor antigen background only (F1.BALB/c). NK cells from selected BM transplantation (BMT) recipients were either depleted ( $\alpha$ -NK1.1) transiently at the time of transplantation or permanently until the end of follow-up. All BMT recipients received skin grafts from the same donor to assess tolerance.

**Results:** Tolerance to BALB/c derived skin allografts could neither be achieved through permanent NK cell depletion (BALB/c) nor in the absence of NK cell alloreactivity (F1.BALB/c). However, if the burden from MiHAs was reduced (CB6F1) or absent (B10.D2), robust tolerance was obtained in stable mixed chimeras. By all means, NK cells impeded the induction of mixed chimerism if MHC barriers were crossed (BALB/c, B10.D2).

**Conclusion:** Therefore, we propose that MHC disparities provoke NK cell mediated BM rejection in non-irradiated recipients treated solely with costimulation blockade and rapamycin while MiHA disparities are a major barrier to tolerance induction towards solid grafts in mixed chimeras.

020

**TETRAHYDROBIOPTERIN MOBILIZES MAST AND REGULATORY T-CELLS IN A MURINE HEART TRANSPLANTATION MODEL**

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**Background:** Tetrahydrobiopterin (BH4) has been shown to attenuate acute cellular rejection in a mouse model of heart transplantation independently from its cofactor activity on nitric oxide synthases. So far, the underlying mechanisms are still unknown. Herein, we wanted to further dissect the immunosuppressive property of BH4.

**Methods:** We used a fully MHC mismatched (C3H/He to C57BL/6) mouse heart transplantation model. Either BH4 (50 mg/kg b.w.) or Cyclosporine A (CsA, 15 mg/kg b.w.) was administered to the recipients for 6 days. Syngeneic grafts and untreated allografts served as controls. Six days post-transplantation, the graft function was assessed by palpation and inspection, the severity of acute rejection was defined by histopathological analysis according to the ISHLT score, and splenocytes were analysed by flow cytometry.

**Results:** The median graft functioning score was significantly higher in BH4 treated compared to untreated animals ( $p < 0.01$ ) and was comparable with CsA treated ( $p = ns$ ) as well as with syngeneic animals ( $p = ns$ ). Severe rejection was diagnosed in untreated allografts, while mild rejection was found in CsA treated and syngeneic grafts ( $p < 0.01$  and  $p < 0.03$ , respectively). BH4 treated grafts ranged from mild to severe lymphocytic infiltrates ( $p = ns$ ). In the spleen of control, CsA treated and BH4 treated animals, dendritic cells and NK cells showed comparable frequencies ( $p = ns$ ). Interestingly, BH4 treated animals showed a substantial increase in cytotoxic T cells ( $p < 0.05$ ), however, displaying lower CD28 expression ( $p < 0.05$ ). Of note, mast cells and regulatory T cells were significantly increased in BH4 treated animals compared to control and CsA treated animals ( $p < 0.05$ ).

**Conclusions:** BH4 treatment leads to an increased mobilization of mast cells and regulatory T-cells which are known to create a functional tolerogenic unit. This finding points to BH4 as a potential new agent for tolerance induction.

**NOVEL BIOMARKERS IN ORGAN TRANSPLANTATION**

021

**MOLECULAR MICROSCOPE (MMDX) IN HEART BIOPSIES – INSIGHT FROM THE INTERHEART STUDY?**

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**Background:** Histopathology of endomyocardial biopsies (EMB) is still the gold standard for diagnosis of an acute rejection in heart transplantation. Several studies have described a discordance between biopsy results if evaluated by different pathologists (Crespo-Leiro, transplantation 2012). The Molecular Microscope (MMDx) is a new technology to analyze biopsies according to molecular diagnostics via microarray technology. The aim of this study was to compare conventional pathology reports with MMDx results in biopsies after cardiac transplantation.

**Methods:** The INTERHEART study consortium is an international multicenter study group evaluating MMDx technology in a prospective observational study. For the INTERHEART study group, one additional biopsy specimen was taken and sent to Transcriptome Sciences Inc., Edmonton, Canada, in RNA later for evaluation with MMDx. Conventional pathology results were graded according to ISHLT criteria for cellular rejection (ACR) and ISHLT consensus for antibody mediated rejection (ABMR). MMDx results were defined as higher probability for ACR and ABMR (>20% archetype score positive). Concordance and discordance of results were analyzed.

**Results:** A total of 127 EMB specimens were evaluated. 14 were excluded due to poor quality of material. 50 biopsies were ISHLT grade 0R (44%), 58 (51%) were 1R and 5 (5%) were 2R. Only 27 biopsies (24%) showed ACR in the MMDx. Concordance with conventional pathology was seen in 44 (88%) of 0R and 4 (80%) of 2R results, whereas only 11 (22%) showed concordance in 1R results. 93 (82%) biopsies were AMR:0 and 20 (18%) showed signs of AMR (ISHLT grade: 1h, 1i, 2). Concordance was seen in 63% (59) of results in AMR:0 and in 75% (15) of AMR ≥1 results.

**Conclusion:** There is a discrepancy of pathological results and MMDx results. In ACR most discrepancy was seen in 1R biopsies and in 37% of

biopsies without AMR and 25% with AMR. Further analysis will be needed to clarify these discrepancies.

022

**TORQUE TENO VIRUS LEVEL IS ASSOCIATED WITH SUBCLINICAL ALLO-REACTIVITY AFTER KIDNEY TRANSPLANTATION, A PROSPECTIVE OBSERVATIONAL COHORT STUDY**

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**Background:** Graft rejection is the major cause of late organ dysfunction after kidney transplantation. Current non-invasive monitoring strategies are not sufficient to detect patients with ongoing allo-reactivity. Torque Teno virus (TTV) level reflects the immunocompetence of its host and is able to predict clinically overt rejection.

**Methods:** To analyse the association between TTV and subclinical kidney allo-graft rejection, an interim analysis of the prospective, observational "TTV POET" cohort study (DRKS00012335) was performed including all data available until 31.1.2019. All available 12 month protocol allograft biopsies of all consecutive recipients of a kidney allograft transplanted at our centre since 01.12.2016 were included (n = 308). Biopsy results were analysed according to current BANFF classification in the context of peripheral blood TTV levels quantified by PCR.

**Results:** A total of 47 allo-graft protocol biopsies were performed at a median of 12.5 month post-transplantation (IQR 12.1–13.5). All recipients had stable graft function at the time of biopsy with a median eGFR of 57 (IQR 45–69; MDRD equation) and a urinary PKR of 92 (IQR 67–188). A total of 20 recipients (43%) had histological evidence of acute allo-reactivity (suspectious/borderline for acute TCMR, n = 16; ABMR, n = 3; TCMR Typ I, n = 1). TTV level quantified at the day of biopsy was lower in recipients with allo-reactivity compared to recipients without such lesions. The risk for allo-reactivity increased by 11% with every log level decrease in TTV copies/mL (RR 0.89, 95% CI 0.85–0.93;  $p < 0.001$ , generalized linear model; primary outcome). Differences in TTV levels were evident not only at the day of biopsy, but more than 6 weeks earlier (median 44 days, IQR 34–54).

**Conclusion:** Our data suggest an association between TTV level and subclinical allo-reactivity at 12 months after kidney transplantation. Future studies will have to test the effect of TTV-guided immunosuppression to reduce subclinical rejection.

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**TORQUE TENO VIRUS DNA LOAD AFTER HEART TRANSPLANTATION AND ITS ASSOCIATION WITH THE STRENGTH OF IMMUNOSUPPRESSION: PRELIMINARY DATA OF A PROSPECTIVE SINGLE-CENTER STUDY**

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**Background:** Long-term survival after heart transplant is still limited due to immunological and drug-related adverse events. Immunosuppressive therapy is solely managed via pharmacokinetic analysis and clinical events. TTV (Torque Teno Virus) is a small single-stranded DNA virus associated with increasing viral load under immune compromising conditions. Studies in both kidney and lung transplantation have already shown that the level of plasma TTV – DNA load is associated with the magnitude of immunosuppression. The aim of this prospective observational study was to analyze TTV viral load in patients after heart transplantation (HTX).

**Methods:** We prospectively determined the TTV load in 50 heart transplant patients. Samples were collected at pre-transplant and each HTX visit in the out-patient clinic. Viral load analysis was performed by PCR from plasma or serum on the Department of Virology. TTV viral load was compared between pre-transplant and peak levels post-transplant. Pre-TX TTV load was compared between different patient groups and between different immunosuppressive protocols after transplantation.

**Results:** Patients were transplanted between 1/2016 and 6/2018. Median age at transplant was 60 (42–67) years and 38% were female. 50% (n = 25) of patients were transplanted due to ischemic disease, 44% (n = 22) due to dilative cardiomyopathy and 6% (n = 3) due to other disease. 16% of patients were bridged with a mechanical assist device (n = 8). Pretransplant TTV levels were  $4.4E+00 \pm 2.03E00$  cps/mL and significantly increased to  $9.39E+00 \pm 0.75 E+00$  ( $p < 0.001$ ) at the TTV peak levels at a median time of 121 (92–185) days post-transplant. Pretransplant, VAD bridged patients had significantly higher TTV loads than non-bridged patients ( $4.02 \pm 1.97E+00$  vs.  $5.93 \pm 0.63 E+00$ ,  $p = 0.023$ ). This difference disappeared after 90–120 days post-transplant (120 days: VAD:  $8.72 \pm 0.74 E+00$  vs. no VAD:  $8.49 \pm 1.17$



E+00,  $p = n.s.$ ). Cyclosporine treated patients had significant lower TTV loads ( $0.47 \pm 1.90$  E+00) compared to tacrolimus treated patients ( $2.52 \pm 5.64$  E+00,  $p < 0.001$ ).

**Conclusion:** TTV viral load increases significantly after heart transplantation and reaches its peak after 90–120 days. VAD pretransplant has an influence of TTC viral load and the choice of calcineurin inhibitor drug seems to be associated with differences in TTV viral load. TTV viral load might be useful as a biomarker for the state of immunosuppression.

#### 024 THE VALUE OF DARC EXPRESSION AS DIAGNOSTIC MARKER IN RENAL TRANSPLANT BIOPSIES

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**Background:** Systematic gene expression profiling of renal allograft biopsies revealed duffy antigen receptor for chemokines (DARC) as one of the genes most strikingly upregulated in antibody-mediated rejection (ABMR). Besides being a blood group antigen, DARC is also associated with endothelial injury. We wanted to determine if immunohistochemistry (IHC) for DARC might serve as diagnostic marker for active ABMR, especially in diagnostically equivocal conditions like C4d negative ABMR.

**Methods:** For this study, we took 86 renal allograft biopsies that were performed during a prospective clinical trial (BORTEJECT Study) with detailed patient and biopsy characteristics available (including gene expression data). IHC for DARC was done on 2  $\mu$ m paraffin sections using a mouse monoclonal anti-human DARC-Fy6 antibody. DARC positive staining was assessed along peritubular capillaries (PTC) and the distribution of the cortical positive stained PTC was further evaluated.

**Results:** 82 biopsies were able to be evaluated for expression of DARC that was mainly observed in peritubular capillaries (PTC) and in small venules and arterioles. 61 biopsies showed positive DARC staining in  $\geq 5\%$  of PTC, mainly located in areas of interstitial fibrosis or inflammation. Most of the ABMR cases were DARC positive ( $n = 40$  vs.  $n = 7$ ,  $p = 0.01$ ), but a substantial amount of biopsies without signs of rejection or borderline lesions still showed DARC positive PTC. Interestingly, C4d positivity was not associated with DARC positivity ( $p = 0.365$ ). On a molecular level, we see a significant difference of DARC gene expression in DARC positive vs. negative biopsies with higher DARC gene expression linked to more DARC positive PTC in biopsies (log scale:  $8.68$  ( $7.91$ – $9.32$ ) vs.  $7.52$  ( $6.99$ – $8.14$ ),  $p < 0.001$ ;  $r_s = 0.546$ ,  $p < 0.001$ ).

**Conclusions:** DARC expression on endothelial cells determined by IHC generally matches DARC gene expression and is associated with ABMR. However, the fact that DARC expression could also be observed in biopsies without signs of rejection limits its value as diagnostic marker for ABMR.

#### 025 HYPERSPECTRAL IMAGING – FIRST APPLICATION IN HUMAN KIDNEY TRANSPLANTATION

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**Introduction:** Medical Hyperspectral Imaging (MHIS) is capable to offer quantitative diagnostic information about tissue pathology, morphology and composition based on the spectral characteristics of different tissue. To date it has not been applied to human solid organ transplantation.

**Material Methods:** Acquisition of hyperspectral images of different components (parenchyma, ureter) of human kidney allografts were taken early after reperfusion and after ureteroneocystostomy using the TIVITA<sup>®</sup> camera device. Images were recorded and analyzed using HSI acquisition software generating oxygen saturation levels (StO<sub>2</sub>), near infrared perfusion indices (NIR), organ hemoglobin indices (OHI) and tissue water indices (TWI) of explored tissues.

**Results:** Four consecutive kidney allografts were assessed in this pilot trial. Assessed Parameters were as follows: (StO<sub>2</sub>: 76.5%; range: (67.2–80.0%)) (NIR: 0.69; range: (0.48–0.79)) (OHI: 0.67; range: (0.45–0.85)) and (TWI: 0.65; range: (0.56–0.74)). A fifth patient was investigated 3-month post-transplant suffering from ureter necrosis. Intraoperative TIVITA<sup>®</sup> imaging displayed marked differences in NIR, OHI and TWI parameters allowing to distinguish viable from necrotic tissue. This assessment had a key impact on operative strategy. A sixth patient scheduled for transplant nephrectomy due to chronic rejection also displayed considerable differences in all assessed parameters when compared to vital organs recorded early after reperfusion.

**Conclusion:** Hyperspectral imaging is a novel tool suitable for non-invasive assessment of kidney allografts early after reperfusion. It allows to identify areas with reduced oxygen supply and perfusion deficits. Further clinical application might focus on prediction of early and future organ function.

## LIVER

#### 026 ALPHA-FETOPROTEIN ADJUSTED UP-TO-SEVEN CRITERIA ARE ASSOCIATED WITH FAVORABLE SURVIVAL AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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**Background:** The Milan criteria (1 nodule  $\leq 5$  cm or  $\leq 3$  nodules  $\leq 3$  cm, no vascular invasion, no extrahepatic manifestation) are recommended to select hepatocellular carcinoma (HCC) patients for liver transplantation (LT). The evaluation of the utility of broader criteria, such as the “alpha-fetoprotein-adjusted Up-To-Seven” (AFP-UTS) is currently ongoing. In this study, we investigated recurrence and overall survival (OS) after liver transplantation (LT) according to AFP-UTS and Milan criteria. We also evaluated the correlation between radiological staging before LT and pathological staging on explant histology.

**Methods:** Adult HCC patients undergoing orthotopic deceased donor LT at the Medical University of Vienna between 1997 and 2014 were retrospectively analyzed.

**Results:** Among 166 patients included, 127 (77%) fulfilled both Milan and AFP-UTS criteria, according to last radiological imaging before LT. For each group, additional 12 patients were identified, resulting in 139 (84%) Milan-in patients in total and 139 (84%) AFP-UTS-in patients in total. 15 patients (9%) fulfilled neither Milan nor AFP-UTS criteria. Median OS of patients within AFP-UTS was 126.9 months vs. 34.2 months outside AFP-UTS (5-year survival rate 71% vs. 43%;  $p = 0.104$ ). 5-year recurrence rate was significantly lower in patients fulfilling the AFP-UTS criteria (18%) than in those exceeding AFP-UTS (64%;  $p < 0.001$ ). Of the 139 patients within AFP-UTS on imaging, 25 (18%) had vascular invasion according to explant histology. Of the 139 patients within Milan criteria on imaging, 24 (17%) had vascular invasion and 47 (34%) were outside Milan according to explant histology. In the subgroup of “radiologically Milan in” patients, the 5-year survival rate was lower in patients with vascular invasion on explant histology (76% vs. 49%;  $p = 0.270$ ) and the 5-year recurrence rate was significantly higher (14% vs. 43%;  $p = 0.002$ ).

**Conclusions:** The overall survival of patients fulfilling the AFP-UTS criteria was favorable in our cohort with a 5-year survival rate above 70%. Vascular invasion according to explant histology is associated with worse outcome after LT. Neither Milan nor AFP-UTS criteria are able to rule out vascular invasion with absolute certainty.

#### 027 THE CHANGES OF TRANSAMINASES, LACTATE DEHYDROGENASE AND PH LEVELS DURING NORMOTHERMIC LIVER PRESERVATION CORRELATE WITH EARLY ALLOGRAFT DYSFUNCTION

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**Background:** Normothermic liver preservation (NMP) has become an established tool to preserve livers in a near-physiological environment. Currently, decreasing lactate and physiological pH-levels are the main parameters used as a decision-making aid to transplant or not to transplant a liver. Our aim was to analyse markers in the perfusate and their impact on initial liver function (ILF) post-transplant.

**Methods:** Perfusates from all livers preserved on an NMP-device were collected throughout the perfusion period at four different time points. Delta values were correlated with the occurrence of early allograft dysfunction (EAD). A p-value  $< 0.05$  was considered significant.

**Results:** Between February 2018-May 2019, 26 livers from deceased donors were transplanted after NMP. Four livers came from donors after circulatory death (DCD), seventeen (65.4%) from ECD. The mean  $\pm$  SD recipient and donor age was  $60 \pm 9.2$  and  $57.3 \pm 17.1$  years. CIT was  $6.7 \pm 2.4$  h; overall preservation time was  $20.3 \pm 7$  h. Six patients (23.1%) received a retransplant. EAD occurred in 6/26 (23.1%) patients. Overall, median peak-AST was 963 U/L (221–8944). Recipient and donor demographics, as well as ischemia and anhepatic times were not significantly different between patients with ILF and EAD, neither were they different between patients developing peak-AST-values higher or lower than the median.

Significant difference between EAD and ILF were delta-values of AST, ALT and LDH; the higher the transaminases and LDH at the end of perfusion, the more likely the occurrence of EAD and high peak-AST-levels;  $p < 0.001$ , Spearman's correlation-coefficient ( $r_s$ ) = 0.780.

The pH-values after 1 h and at the end of NMP correlated significantly with EAD,  $p = 0.027$  and  $0.012$ ,  $r_s = -0.441$  and  $-0.506$ .

**Conclusions:** Testing viability using perfusate parameters over time is possible. Increased transaminases and LDH, as well as lower pH-levels early after perfusion start, have to be considered as important factors correlating with EAD. Future comparisons with perfusate levels of discarded NMP livers will shed more light into viability assessment of livers.

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### IMPACT OF DUAL OXYGENATED HYPOTHERMIC EX VIVO LIVER PERFUSION ON BILIARY COMPLICATIONS

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**Background:** Ex vivo liver perfusion has been implemented in several transplantation centres as an alternative to static cold storage. The aim of this study was to investigate a potential decrease of biliary complications after transplantation of livers subjected to dual oxygenated machine perfusion (DHOPE).

**Methods:** DHOPE (Liver Assist device) has been routinely used at the Medical University of Vienna since May 2018. Patients who received a perfused organ were compared to a control group transplanted in the same time period and whose grafts were stored using static cold storage (SCS).

**Results:** In total, the first 20 patients who received a perfused organ were compared to 22 controls. Bilirubin levels after LT peaked at 5.64 mg/dL (IQR 5.7 mg/dL) in the perfusion group vs. 6.95 mg/dL (IQR 6.74 mg/dL) in the control group ( $p = 0.44$ ). Alkaline phosphatase levels after LT peaked at 144 U/L (IQR 122 U/L) in the perfusion group vs. 128 U/L (IQR 108 U/L) in the control group ( $p = 0.98$ ). After 3 months both levels normalized in both groups. In the perfusion group, 3/20 (15%) patients developed biliary complications – two patients had an early biliary leak and one patient developed bile duct necrosis 2.5 months after LT. In the control group, 4/22 (18%) developed biliary complications within the first 3 months (two patients had an early biliary complication and 2 showed ITBL). MRCPs performed 3 months after LT showed any abnormal findings in 4 patients in the perfusion group and 4 patients in the control group, with clinical relevance in 1/4 (perfusion group) and 2/4 (control group).

**Conclusion:** Dual oxygenated hypothermic ex vivo perfusion of liver grafts was safe and showed in this pilot study a similar proportion of biliary complication compared to static cold storage.

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### EARLY HEPATIC REARTERIALISATION – A GRAFT SAVING PROCEDURE

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**Background:** Hepatic artery thrombosis (HAT) following liver transplantation (LT) is a life threatening condition and thus it is an accepted indication for reLT; however, in some cases revascularisation, even when delayed, is possible.

**Methods:** A total of 145 patients underwent LT between January 1st, 2014 and July 7th, 2019 in our center. Out of these, 6 pts. (3 male, 3 female) underwent reLT. While reLT was necessary in 5 pts for primary graft failure, there was HAT in 1 pt.

In 4 pts. (3 male, 1 female) early HAT occurred and reconstruction with either autologous (saphenic vein) or heterologous (iliac artery) vascular graft was performed successfully. The median delay between diagnosis of HAT and revascularisation was 6.25 h (2–30).

**Results:** While 1- and 2-years overall survival was 100% after rearterialisation, it was only 83.3% after reLT. Biliary complication occurred if pts. underwent arterial reconstruction after more than 2.5 h after diagnosis (50% of cases).

**Conclusion:** HAT without can be managed surgically with great success especially if diagnosed early. Autologous saphenic vein graft and heterologous iliac arterial graft are suitable for hepatic artery reconstruction. Screening of the arterial perfusion of the graft on at least a daily basis by Doppler-ultrasound during the first postoperative week may be graft saving.

030

### GENDER DISCRIMINATION VIA MELD-BASED LIVER ALLOCATION

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**Background:** MELD was implemented to guarantee urgency-based and fair organ allocation. Nonetheless men are outnumbering women as liver

transplant recipients. The aim of this study was to analyze gender disparities in liver transplantation particularly with regard to organ allocation in a nationwide cohort.

**Methods:** All liver transplantations – excluding pediatric recipients, combined organ transplantation and living donors – from 2005 to 2015 in Germany were assessed retrospectively using the data record of Eurotransplant.

**Results:** 9832 liver transplantations fulfilled all criteria in the investigated period. Nearly two thirds (6466; 65.8%) of all recipients were male. This percentage was even higher in patients allocated by regular allocation without high urgency status (male 68.7%).

Latest laboratory MELD score as well as MatchMELD score were higher in women compared to male recipients (23 vs. 18;  $p < 0.001$  and 28 vs. 26,  $<0.001$ , respectively). Men on the other side were more likely to have an exceptional status compared to women (30.9% vs. 23.4%;  $p < 0.001$ ) as 80% of all transplantations for hepatocellular carcinoma occurred in men. In contrast, common indications for women are not considered for standard exceptions (e.g. PBC – 77% females). Besides this discrimination in indications laboratory values of the MELD score differed by gender. Although women showed better serum creatinine values (1.38 mg/dL vs. 1.6 mg/dL;  $p < 0.001$ ) eGFR was significantly lower (65.9 vs. 69.2;  $p < 0.001$ ). Despite being sicker, women do not generate high MELD scores due to lower muscle weight. Therefore, their Bilirubin (11.02 vs. 8.77;  $p < 0.001$ ) and INR (2.02 vs. 1.72;  $p < 0.001$ ) had to achieve higher values before getting organ offers. The mean difference in creatinine values corresponded to approximately two points in the labMELD score.

**Conclusions:** There is a significant gender inequity in liver transplantation recipients. Probably this can be partially explained by varying incidences of liver diseases, but MELD based allocation seems to aggravate the injustice. A critical analysis whether access to liver transplantation is equal for all genders is needed.

## ORGAN ALLOCATION AND PERIOPERATIVE MANAGEMENT

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### INCREASING ORGAN DONATION: A CONSENSUS BETWEEN EXPERTS FROM FOUR DIFFERENT COUNTRIES AND HEALTH CARE SYSTEMS FROM AUSTRIA, GERMANY, SPAIN AND THE UK

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**Background:** Post-mortal organ donation rates and organizational approaches to organ donation differ drastically between countries at a similar level of health care. Expert opinions from Austria, Germany, Spain and the UK on the respective system and practice of organ donation can help to improve organ donation.

**Methods:** Opinions from intensive care nurses, physicians, transplant coordinators and transplant surgeons in the four countries were obtained in semi-structured interviews followed by qualitative analysis.

**Results:** Interviews show that a variety of factors can have a beneficial effect on organ donation rates, e.g. standardized screening for potential donors, a standardized family approach and mandatory training for family approach teams. The role of ICU doctors is crucial, but they need to be supported by full-time in-house special nurses for organ donation who organize donor evaluation, transport logistics and coordination and by pastoral workers, if required. Failure to report potential organ donors should have consequences, but incentives are not effective. Awareness campaigns should encourage families to discuss organ donation. An opt-out system is likely to stimulate family



discussions. Public trust can be achieved by full transparency in organ donation and transplantation and by prevention of scandals. Broad public consensus on the concept of brain death and donation after cardiac death is a sound basis for organ donation. Standards and best-practice procedures need to be regulated and supervised by state authorities.

**Conclusions:** A consensus between experts from four different countries and health care systems within Europe can be achieved easily on how to improve organ donation systems and organ donation rates. This advice should be used to reform organ donation systems that lack efficiency and effectiveness as well as transparency resulting in low realized organ donation rates per capita with drastic consequences for patients in need of organ transplantation.

### 032 ROLE OF SEROTONIN AS A MARKER FOR GRAFT QUALITY IN LIVER TRANSPLANTATION – A COMPARISON BETWEEN ACCEPTED AND REJECTED DONORS

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**Background:** Multiple factors influence the quality of organ donors in liver transplantation. In the setting of liver resection, current research demonstrated the essential effect of platelets and platelet derived growth factors, especially serotonin, on liver regeneration. Therefore, we evaluate the role of serotonin in liver transplantation and its effect to predict organ quality.

**Methods:** To quantify the intra-platelet serotonin amount blood samples of potential liver donors were drawn before organ harvest and serum and plasma were analyzed through serotonin enzyme-linked immunosorbent assays (ELISA). The calculation of intra-platelet serotonin resulted from subtraction of plasma from serum serotonin levels. Finally, during organ harvest the donors were split into two groups, harvested (LTX) and rejected (No-LTX) liver donors.

**Results:** In total 12 harvested and 18 rejected organ donors were analyzed. Serum serotonin and intra-platelet serotonin were higher in the group of harvested organ donors compared to rejected organ donors. Serum LTX: 105, 56 ± 56.52 ng/mL vs. Serum No-LTX: 49.03 ± 29.15 ng/mL, IP-Serotonin LTX: 103.38 ± 56.37 ng/mL vs. IP-Serotonin No-LTX 44.71 ± 29.73 ng/mL.

In contrast to that plasma serotonin of rejected organ donors was higher than in the group of harvested organ donors. Plasma No-LTX: 5.09 ± 3.62 ng/mL vs Plasma LTX: 2.18 ± 0.79 ng/mL.

**Conclusion:** The lower levels of serum and intra-platelet serotonin of rejected liver donors may be an evidence for worse graft quality in this group. Chronic platelet activation and thereby chronic serotonin release due to worse organ function might explain the lower serotonin levels compared to finally transplanted grafts of "good" quality.

### 033 OLT IN PATIENTS WITH POSITIVE CROSSMATCH – A RETROSPECTIVE SINGLE-CENTER STUDY

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**Background:** A positive crossmatch is usually considered a contraindication to all solid organ transplantations except orthotopic liver transplantation (OLT). There are conflicting reports in the literature regarding the effects of a positive crossmatch on post-transplant outcomes. While some authors suggest a link between positive crossmatch cases and the presence of donor specific antibodies (DSA) regarding allograft survival and graft complications, others were not able to duplicate those findings. Clinical practice has not changed to this date. Patients with positive crossmatch continue to be transplanted. The goal of this retrospective single center analysis is to evaluate the influence of positive crossmatch on relevant clinical outcome parameters such as graft survival, re-transplantation, allograft rejection and biliary complication.

**Methods:** In this retrospective single center study 53 patients who received OLT after positive crossmatch in the time period between 2002 and 2017 were identified. Outcome analysis based on available data from our liver transplantation database was performed for these patients. Statistical analysis was performed using Graph Pad Prism and SPSS.

**Results:** Median graft survival was 48 months. 16 patients (30.2%) died while 5 patients (9.4%) underwent liver re-transplantation. 12 patients (22.6%) developed early allograft dysfunction. 8 patients (15.1%) developed vascular complications. 11 patients (20.8%) had acute or chronic allograft rejection while 20 patients (37.7%) developed biliary complications. 31 patients (58.5%) received induction therapy. Univariate and multivariate analyses identified a documented episode of allograft rejection as the only relevant predictor regarding the development of biliary complications.

**Conclusions:** Based on our preliminary results, further analysis and risk stratification are needed for this patient cohort. The potential of induction therapy to mitigate immunologic injury caused by a positive crossmatch needs to be defined.

### 034 RISK FACTORS FOR PRIMARY POOR FUNCTION IN LIVER TRANSPLANTATION: A RETROSPECTIVE SINGLE-CENTRE ANALYSIS

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**Background:** Primary poor function (PPF) results in poor outcomes. Recipients who develop PPF experience higher mortality and graft loss rates. The aim of this analysis was to assess PPF as an intermediate outcome measure in a large single centre cohort and to evaluate the individual effect of each variable on patient and graft survival.

**Methods:** PPF was defined as the presence of one or more of previously defined postoperative laboratory analyzes: bilirubin ≥10 mg/dL on day 7; INR ≥1.6 on day 7, AST >2000 IU/L on day 1–7. The effect of PPF on recipient and graft survival was analyzed and risk factors for PPF were assessed using multivariate analyzes and the Kaplan-Meier method.

**Results:** The incidence of PPF was 31.3%. 1-, 3-, 5-year graft and patient survival were worse in patients with PPF than in those without ( $p < 0.01$  at all time points). However, the majority of patients with PPF fulfilled the AST criterion ( $n = 187$ ; 24.3%). Considering patients meeting the AST criterion (singular or combined) similar survival rates at 1-, 3-, and 5-year ( $p = 0.366$ , 0.21, 0.299 for patients and  $p < 0.05$  for grafts) respectively could be obtained compared with the no-PPF group. Multivariate analysis showed associations between PPF and re-transplantation, recipient hepatitis-C-positive status, ( $p < 0.05$ ), recipient graft Child Score ( $p < 0.01$ ), cold ischemia time ( $p < 0.05$ ), anastomosis time, post-operative hematoma ( $p < 0.01$ ), donor BMI, donor graft steatosis, donor GGT ( $p < 0.01$ ). Patients with PPF had a significantly longer hospitalisation (30.8 ± 23.3 days compared to 26.5 ± 19.8 days,  $p < 0.01$ ).

**Conclusion:** Recipient-, surgery- and donor-related factors have been associated with PPF. Considering the rapid evolvement in LTX, re-examination of the current definition of PPF and individual weighing of involved parameters should be evaluated.

### 035 INFECTION SAFETY OF LOW-DOSE ATG INDUCTION IN LIVER TRANSPLANTATION

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**Background:** CMV PCR positive episodes, urinary tract and bronchopulmonary infections are typical complications of immunosuppression and are associated with increased mortality after liver transplantation. Systematic analyses of the effects of routine low-dose ATG induction therapy on infectious complications after liver transplantation are lacking. This study analyses the influence of low-dose ATG induction (0.5 to 1.0 mg/kg/day for 3–4 days) on CMV PCR positive episodes, urinary tract and/or bronchopulmonary infections within the first month after liver transplantation.

**Methods:** Patients with primary liver transplantation performed at Medical University Graz between the 1.1.2007 and the 31.12.2018 were included. Patients with additional kidney transplantation within the first year after liver transplantation were excluded leading to a cohort of 211 patients for the investigation of independent influences of ATG on urinary tract and/or bronchopulmonary infections and CMV PCR positive episodes within the first month after liver transplantation.

**Results:** 131 patients received ATG induction (62.1%). Multivariable binary logistic regression revealed that ATG induction had no independent, significant influence on urinary tract and/or bronchopulmonary infections (OR = 1.052,  $p = 0.890$ ) while it independently and significantly increased the risk of CMV PCR positive episodes (OR = 4.648,  $p < 0.001$ ) within the first month. A D-/R- CMV match was revealed as an independent and significant protective factor for CMV PCR positive episodes within the first month after transplantation (OR = 0.070,  $p < 0.001$ ). Obese patients with a BMI >25 kg/m<sup>2</sup> were identified to be exposed to an independently and significantly increased risk of infection.

**Conclusion:** Low-dose ATG induction is safe regarding the risk of early urinary tract and bronchopulmonary infections but is an independent and significant risk factor for CMV PCR positive episodes within the first month after liver transplantation. Patients with low-dose ATG induction should therefore receive routine CMV prophylaxis, which is even more important in patients with a BMI >25 kg/m<sup>2</sup>.

036

**USE OF INDUCTION THERAPY IN PEDIATRIC HEART TRANSPLANT RECIPIENTS IN SWITZERLAND**

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**Background:** Evaluation of induction therapy practice in a national pediatric heart transplant program.

**Methods:** Retrospective analysis of the Swiss Transplant Cohort Study (STCS). Ethical approval as well as approval by the STCS were granted.

**Results:** Between 05/2008 and 6/1/2018 347 heart transplantations were registered within the database. Out of these 32 transplants were done in 31 patients (11♂, 20♀) <19 years of age in four centers. Twelve patients (38%) were bridge with a VAD to transplant. One patient received a re-transplant. There were no combined transplants with other organs.

Mean age at time of transplant was 7.6 years (±1.1). 11 patients were on a VAD prior to transplant. Primary diagnosis were: DCMP (22), CHD other than DCMP (4), other (5). All donors were brain dead donors. Mean Ischemic time was 123 min (±13.8). Compared to adults where 4.1% of patients received no induction therapy it was given at a median of 4 days (1–63) in all patients of the study group (9 patients received IL2 receptor antibodies, 23 anti-thymocyte globulin) as well as corticosteroids. Corticosteroids were stopped after a median of 261 days (range 1–1079). There were 7 donors EBV+ on EBV– recipients, whereas 9 patients were constellation dCMV+, rCMV–. Median follow up time was 2.96 years ranging from 106 days to 8.1 years. There were no PTLD in the follow up. Six patients died within the observed time period.

**Conclusion:** Induction therapy is widely accepted in Switzerland. Negative long-term effects especially PTLD were not reported.

**KIDNEY**

037

**SERUM 25-HYDROXYVITAMIN D AND 1,25-DIHYDROXYVITAMIN D ARE NOT ASSOCIATED WITH MAJOR INFECTIONS DURING THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION**

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**Background:** Kidney transplantation (KT) is the most effective way to reduce morbidity and mortality risk of patients with end-stage kidney disease. However, higher risk of infections is encountered in kidney transplant recipients (KTR). The pleiotropic role of vitamin D has been widely investigated over the past decades, including its effects on the immune system. 25-hydroxyvitamin D (25(OH)D) requires conversion to its active metabolite, calcitriol, for most biological effects. Recent studies have reported an increased risk of infection for vitamin D-deficient KTR, but studies investigating the association of both 25(OH)D and 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D) on major infections of KTR are lacking.

**Methods:** Serum 25(OH)D (n = 343) and 1,25(OH)<sub>2</sub>D (n = 144) were measured in a retrospective cohort of KTR (2005–2015) within 3 months after KT, respectively. Data on clinical characteristics, infection incidence, infection-related hospital admissions and mortality data were recorded during the first year after KT. The primary outcome was infection-related hospital admission after KT.

**Results:** Median 25(OH)D and 1,25(OH)<sub>2</sub>D concentrations were 23.5 ng/mL (IQR:15.2–31.1) and 63.5 pg/mL (IQR:31.0–97.5) and 248 patients (72.3%) were vitamin D insufficient (25(OH)D<sub>3</sub> <30 ng/mL). Incidence of infections did not differ between the patients with sufficient and insufficient 25(OH)D and 1,25(OH)<sub>2</sub>D concentrations (all p > 0.05, respectively). 25(OH)D insufficiency and the lowest tertile of 1,25(OH)<sub>2</sub>D were not associated with increased hospital admissions due to major infection-related complications (hazard ratio [HR]:0.90; 95% confidence interval [CI]:0.48–1.71 and HR:1.16; 95%CI:0.48–2.83). Only 6 patients (1.75%) died due to infections. All-cause mortality during the first post-transplant year was also not associated with 25(OH)D insufficiency (HR:1.27; 95%CI:0.38–4.28).

**Conclusion:** Serum 25(OH)D and 1,25(OH)<sub>2</sub>D concentrations were not associated with infection-related hospital admissions. Our data do not argue for an association between vitamin D status and infections during the first year after KT. Data on late onset infections and major infection-related complications associated with vitamin D status should be investigated.

038

**TARGETING CD38 AS A NEW TREATMENT OF ANTIBODY-MEDIATED ALLOGRAFT REJECTION**

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**Background:** Late ABMR is a cardinal cause of allograft failure and loss. Currently, there is no effective treatment for this rejection type. Promising targets are antibody-secreting and/or natural killer (NK) cells, both expressing high levels of CD38. Here, we report the first use of CD38 antibody daratumumab in chronic-active ABMR.

**Methods:** A 50-year-old male kidney allograft recipient was diagnosed with myeloma and ABMR

14 years after transplantation [g+ptc = 3; cg = 3; 2 DSA (DQ6/DQA1; MFI: 3761/3702)]. For simultaneous treatment of both diseases, the patient was given a 9-month course of daratumumab. A detailed monitoring comprised serial bone marrow and transplant biopsies (baseline, mo-3, mo-9), the latter including gene expression analysis (MMDx), Luminex-based anti-HLA antibody testing, and immunophenotyping of peripheral blood NK (CD45+/CD3–/CD4–/CD19–/CD56+/CD16var) and antibody-producing cells (CD45var/CD19var/CD138+/CD81var/CD27+/CD56–/CD200–).

**Results:** Daratumumab led to a marked reduction in free lambda light chains (770 vs. 15.7 mg/L) and plasma cell depletion in the bone marrow (20% at baseline vs. <1% CD138+ cells at mo-9). Immunophenotyping revealed a substantial decrease in the number of circulating NK (92 × 10<sup>6</sup> vs. 18 × 10<sup>6</sup> cells/L) and antibody-producing cells (89 × 10<sup>3</sup> vs. 16 × 10<sup>3</sup> cells/L). At the same time, we observed a substantial decrease of total IgG/IgA/IgM and, in parallel, disappearance of DSA. An intriguing finding was an abrogation of microcirculation inflammation, with a molecular shift from fully-active to late-stage ABMR, and a marked reduction of an initially high molecular ABMR score (0.79 to negative). A classifier of transplant glomerulopathy, however, remained unchanged. Renal function remained stable with a decrease in urinary protein excretion (serum creatinine: 2.49 vs. 2.46 mg/dL; protein-creatinine-ratio: 2700 vs. 1480 mg/g).

**Conclusion:** Targeting CD38 may be an effective strategy to counteract ABMR – presumably as a result of NK and plasma cell depletion. Our results support the design of future trials to clarify the role of this innovative treatment concept in organ transplantation.

039

**LEFT VERSUS RIGHT DONOR KIDNEY: OBSERVED CONSEQUENCES OF TRANSPLANTATION EITHER INTO THE LEFT OR RIGHT ILIAC FOSSA**

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**Background:** Data on the consequences of accepting a left versus right donor kidney and transplanting it into either the left or right iliac fossa is lacking. This study evaluates the impact of these decisions on surgical outcome.

**Methods:** This retrospective single-center study analyzed 1262 deceased donor adult kidney transplants into a pristine iliac fossa performed at Hannover Medical School. Multivariable linear regression and logistic regression were used to determine risk factors for prolonged operating time (OT) and complications.

**Results:** Transplantation into the right iliac fossa and anastomosis to the caval or common iliac vein independently reduced OT while lower recipient's age, daytime transplantation, higher BMI and multiple arterial anastomoses significantly prolonged OT as confounders (p < 0.05). Transplantation of right and left donor kidneys into the right iliac fossa was significantly faster (Δmedian: 11:00 min, p < 0.001) without increasing surgical complications. Transplanting left donor kidneys into the right iliac fossa with venous anastomosis to the caval vein or common iliac vein yielded shortest OT (median: 112:30 min). Prolonged OT was associated with an increased risk for venous macro-thrombosis (OR = 1.023, 95%-CI: 1.015–1.031) and arterial micro-thrombosis (OR = 1.012, 95%-CI: 1.000–1.024). Frequencies of observed surgical complications were equally distributed between all four combinations of right or left donor kidneys transplanted either into the right or left iliac fossa.

**Conclusions:** Transplantation should be performed into the right fossa with anastomosis to the caval vein or the common iliac vein to save operating time and to reduce thrombotic complications. Acceptance of a left donor kidney in this situation likely reduces operating time further.

#### 040 PERIOPERATIVE AND SHORT-TERM OUTCOMES OF ROBOTIC ASSISTED LIVING KIDNEY DONATION

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**Background:** Robotic assisted kidney donor surgery represents one of the most advanced surgical techniques for living kidney donation competing for supremacy with totally laparoscopic and laparoscopic hand assisted techniques.

**Methods:** We present our initial experience with 40 consecutive patients who underwent robotic assisted living kidney donation from September 2013 to August 2018 performed with the da Vinci Si surgical platform.

**Results:** Within the last 5 years the amount of robotic assisted living kidney donation almost quintupled. A total of 21 left (52.5%) and 19 (47.5%) right kidneys were used for transplantation. Mean donor age was 53 (range: 28–70). The average total operative time was 151 ± 27 min, with no difference between patients with single (n = 29, 72.5%) 151 ± 27 min or multiple (arterial and/or venous) (n = 11; 27.5%) 150 ± 29 min renal vascular supply. Interestingly, right donor nephrectomy (139 ± 22 min) was significantly faster than left (161 ± 28 min) nephrectomy. No conversion to open surgery needed to be performed. Postoperative complications occurred in five cases. Clavian Dindo grade <IIIb complication occurred in (n = 3) 7.5%, grade IIIb in (n = 2) 5%. Grade IV and V complications did not occur. Mortality was 0%. 13 kidneys (32.5%) were transplanted across the ABO barrier, requiring therapeutic apheresis as well as T- and B-cell directed immunosuppressive therapy. One-year graft survival was 97.5%.

**Conclusion:** Robotic assisted living kidney donation is an emerging minimally invasive surgical technique which facilitates excellent perioperative and short-term outcomes.

#### 041 URINE RECIRCULATION IMPROVES HAEMODYNAMICS AND ENHANCES FUNCTION IN NORMOTHERMIC KIDNEY PERFUSION

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**Background:** The purpose was to compare urine recirculation (URC) and urine replacement with Ringer's lactate in a porcine normothermic kidney perfusion model.

**Methods:** Pigs (n = 10) were allocated to either NKP with URC (n = 5) or NKP without URC (n = 5), where Ringer's lactate replaced urine output. Animals were anaesthetised and both kidneys were retrieved, uninjured. One kidney was placed on NKP after 2 h cold ischaemia time (CIT) and the remaining kidney was static cold stored for 27 h and then placed on NKP. An autologous blood-based perfusate solution, leukocyte-filtered, was used and NKP performed up to 24 h. Perfusion parameters, biochemistry and metabolic parameters were monitored and perfusate, urine and tissue samples were collected.

**Results:** Physiological mean arterial pressures and flows were achieved in perfusions with and without URC, within the first hour of perfusion but remained stable only with URC. Significantly higher arterial flow levels could be achieved with URC; median arterial flow of 319 mL/min with URC vs 226 mL/min in NKP with urine replacement, p < 0.0001. The duration of CIT before NKP start had no impact on arterial flow. Perfusate sodium levels were higher without URC, 129.9 ± 12.3 with URC vs 158.7 ± 19.4 without; p < 0.001. pH was stable at physiological levels only in NKP with URC. Lactate levels, compared within each kidney pair, were lower with URC, 2.55 ± 1.28 vs 6.9 ± 1.6; p < 0.001. The hourly urine output was higher in NKP without URC; 548 mL/h vs 150 mL/h with URC, p = 0.008. The achieved duration of NKP (up to 24 h) was significantly longer in NKP with URC, 17.3 ± 9.2 vs 5.3 ± 1.3 NKP without; p = 0.02. The baseline tubular condition appeared unchanged after NKP with and without URC.

**Conclusion:** Normothermic kidney perfusion using a portable prototype device preserves the parenchymal quality of healthy porcine kidneys with and without URC. Urine recirculation is needed to maintain haemodynamics, perfusate volume and homeostasis and to readily achieve up to 24 h.

#### 042 30 YEARS OF LIVING DONOR KIDNEY TRANSPLANTATION – A SINGLE-CENTER ANALYSIS

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**Background:** Living donor (LD) kidney transplantation provides the best option to maximize long-term transplant outcomes. We herein report our 30 years experience of LD kidney transplantation.

**Methods:** We retrospectively analyzed 333 LD kidney transplants performed at the Medical University of Innsbruck between 1985 and 2016. For descriptive statistical analysis, mean values, absolute and relative frequencies were calculated. Patient and graft survival was evaluated according to Kaplan Meier survival statistics.

**Results:** 87% of patients received their first kidney transplant, and 13% had a retransplant. Preemptive transplantation was performed in 35% of patients. 71% were living-related and 29% were living-unrelated kidney transplants. 3% of transplants were ABO incompatible. The follow-up rate was 86.5% with a mean follow-up of 9 years.

Patient survival was 97.6%, 92.2%, 83%, 72.6%, and 69.5% at 1, 5, 10, 20, and 25 years. Overall graft survival was 96.3%, 84.1%, 69.2%, 38.2% and 26.2% at 1, 5, 10, 20, and 25 years with a median allograft survival of 15 years. Delayed graft function occurred in 7.6% of patients. 34% of patients experienced an acute rejection episode. Postoperative morbidity included surgical complications in 11.1% and infectious complications in 12.6%. 9% of LD kidney transplants developed a post-transplant malignancy, excluding non-melanoma skin cancer.

**Conclusion:** Over a period of 30 years LD kidney transplantation yielded satisfactory long-term patient and graft survival rates. On the strength of stringent follow-up the study adds valuable evidence on the long-term outcomes after LD kidney transplantation.

#### LONG-TERM FOLLOW-UP

#### 043 LOW-DOSE ATG HAS NO INFLUENCE ON PATIENT SURVIVAL, GRAFT SURVIVAL AND CANCER-FREE SURVIVAL AND IMPROVES RENAL OUTCOME IN PATIENTS WITH COMPROMISED KIDNEY FUNCTION AFTER LIVER TRANSPLANTATION

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**Background:** The current indication for ATG induction in liver transplantation is highly controversial. Data on the effects of low-dose ATG induction are lacking. This study therefore investigates retrospectively the safety and benefits of low-dose ATG induction (0.5 to 1.0 mg/kg/day for 3–4 days) in liver transplantation.

**Methods:** Patients with primary liver transplantation at Medical University Graz between the 1.1.2007 and the 31.12.2018 were included. Patients with additional kidney transplantation were excluded from analysis leading to a cohort of 211 patients for the investigation of independent influences of ATG on patient survival, graft survival and cancer-free survival using multivariable Cox regression analysis. The independent influence of ATG on KDIGO-stage improvement of renal function at 6 months after transplantation was investigated using multivariable logistic regression analysis after further exclusion of 31 patients with lack of data for postoperative renal function classified in KDIGO-stages at 6 months after transplant.

**Results:** 131 patients received ATG induction (62.1%). Significant differences between patients with ATG induction versus without ATG induction were identified for the distribution of the indication hepatocellular carcinoma (16.0%, 28.8%, respectively). The distribution of all other pre-transplant variables was not significantly different. Multivariable Cox regression revealed that ATG induction did not have an independent statistically significant influence on patient survival, graft survival and cancer-free survival (p > 0.050). Multivariable logistic regression revealed that a body-mass index (BMI) >25 kg/m<sup>2</sup> (OR = 0.297, p = 0.036), pre-transplant KDIGO-stages (OR = 3.746, p < 0.001) and low-dose ATG induction (OR = 3.636, p = 0.043) had independent significant influences on KDIGO-stage improvement at 6 months after liver transplantation.

**Conclusion:** Low-dose ATG induction is safe in regard to patient, graft and cancer-free survival. Low-dose ATG induction improves renal function after liver transplantation which is more pronounced in patients with compromised renal function prior to liver transplantation and in those patients with a BMI <25 kg/m<sup>2</sup>.



044

### MAGNETIC RESONANCE IMAGING FOR ANALYSIS OF T1-MAPPING-BASED RELAXATION TIME – A NON-INVASIVE TOOL FOR MONITORING OF CHRONIC KIDNEY ALLOGRAFT INJURY

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**Background:** Interstitial fibrosis (IF) represents a key feature of chronic kidney allograft injury. Its quantification relies on biopsy-based evaluation – an invasive and observer-dependent test. One attractive strategy for accurate monitoring of chronic graft injury may be non-invasive, MRI-based T1-mapping. In this prospective study, we evaluated the diagnostic accuracy of T1-mapping in relation to biopsy-scored IF and other lesions reflecting chronic injury.

**Methods:** Based on sample-size calculation, a prospective study was designed to investigate whether T1-mapping can dissect chronic transplant injury in 32 renal allograft patients, undergoing routine allograft biopsies. Patients were eligible for study inclusion after informed consent was given and were subjected to investigator-blinded 1.5T MRIs. Biopsies were analysed following the Banff 2017 scheme, including interstitial fibrosis (ci), tubular atrophy (ct), transplant glomerulopathy (cg), chronic vasculopathy (cv) and IFTA.

**Results:** Among 32 participating patients (mean age 53.9 ± 15.3 years), median ci scores were 2.0 (IQR:1–3). We found significant correlations between cortical T1-relaxation time and ci scores ( $r = 0.388$ ,  $p = 0.028$ ) as well as ct ( $\rho = 0.505$ ,  $p = 0.003$ ), cg ( $\rho = 0.363$ ,  $p = 0.049$ ) or cv ( $\rho = 0.442$ ,  $p = 0.027$ ), respectively. Subjects with moderate or severe IF showed higher T1 relaxation times (1451 milliseconds [ms]; [interquartile range: 1137–1763] vs. 1306 [1115–1538,  $p = 0.004$ ]). Receiver operating curve analysis revealed an area under the curve (AUC) of 0.76 (95% CI:0.56–0.95) for the prediction of ci 2–3. Remarkably, the predictive accuracy of T1-relaxation time was highest in analyses focussing on the biopsied region (ci 0–1: 1238 (1112–1567), ci 2–3 1457 (1195–1580),  $p = 0.003$ ; AUC 0.79 (95% CI:0.60–0.97).

**Conclusions:** These results demonstrate a strong relationship between T1-mapping and features of chronic allograft injury, particularly IF. The finding of superior accuracy from analysis of the biopsied region may indicate sampling error of biopsy-based parameters. Future studies will have to clarify whether T1-mapping can serve as a reliable surrogate endpoint reflecting the course of chronic graft damage.

045

### SECOND PRE-EMPTIVE RENAL TRANSPLANTATION IS NOT ASSOCIATED WITH PROLONGED GRAFT SURVIVAL

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**Background:** First pre-emptive kidney transplantation is associated with prolonged graft survival when compared to patients with dialysis vintage before transplantation. However, for the second pre-emptive transplantation there exists contradictory literature. Therefore, we elucidated if the benefit is still given after the second pre-emptive transplantation.

**Methods:** We identified 1886 patients from the Austrian Dialysis and Transplant Registry (OeDTR) who were transplanted at least two times between 1980 and 2018. Eighty of them received the second transplantation without prior dialysis. We used a multivariable Cox model adjusted for weighted inverse probability of treatment to investigate the association of dialysis vintage with graft survival. The analysis was further adjusted for renal diagnosis, HLA mismatch in loci A, B, and DR, donor status (living, deceased), recipient sex and recipient age.

**Results:** The second pre-emptive transplantation was not associated with a reduced risk of graft loss compared to dialysis vintage (HR: 0.79, 95% confidence interval 0.53–1.19,  $p = 0.264$ ). Of the included covariables, age of recipient, renal diagnosis as well as donor status were associated with graft survival.

**Conclusion:** In the current data set, we showed that second pre-emptive transplantation was not associated with longer graft survival.

046

### SURVIVAL BENEFIT OF PATIENTS UNDERGOING MORE THAN TWO KIDNEY TRANSPLANTS – MOVING TOWARDS CHALLENGING TRANSPLANTATIONS

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**Background:** The best option concerning patient survival, cost effectiveness and quality of life for end-stage kidney disease still constitutes kidney

transplantation. In times of optimizing treatment, we aim to assess whether 3rd, 4th and 5th kidney transplantation (NTx) is reasonable.

**Methods:** A retrospective single-center analysis was performed to assess long-term patient and graft survival of 98 NTx performed for the 3rd, 4th and 5th time. Kaplan–Meier analysis was used to compute overall graft and patient survival. Cox proportional hazard models were employed for uni- and multivariate analysis of demographics and risk factors.

**Results:** A total of 80 3rd, 16 4th and two 5th NTx were performed during the last 40 years. The 1-, 5-, 10- and 20-years graft and patient survival was 87.8%/94.9%, 73.9%/78.6%, 70.1%/75.6% and 47.7%/69.5%. In comparison, 10% superior survival rates were yielded for the 2nd transplant cohort (86.6%/98.6%, 75.6%/93.5%, 69.9%/87.8% and 62.1%/75.0%). In the entire cohort, 24 (24.2%) patients died and 31 (31.3%) lost their graft within the observational period. Risk assessment revealed graft loss as a significant risk factor for patient survival. Considering 5- and 10-years graft survival, a significant difference between standard and extended criteria donor organs was detected (77.5% vs. 54.5%; 74.7% vs. 54.5%). The recipient age did not impact significantly on graft and patient outcome. Organs from donors after cardiac death were not utilized in this cohort.

**Conclusions:** Despite preexisting donor specific antibodies and a challenging surgery, the favorable outcomes after multiple kidney re-transplants emphasize towards these high-risk transplantations when compared to renal replacement therapy. Even patients beyond their 60s seem to benefit from repeated renal transplantations.

047

### SHORT- AND LONG-TERM METABOLIC OUTCOMES IN PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES RECEIVING A SIMULTANEOUS PANCREAS KIDNEY ALLOGRAFT

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**Background:** Simultaneous pancreas-kidney transplantation (SPK) is still the treatment of choice for C-peptide negative patients suffering from insulin-dependent type 1 diabetes mellitus (T1DM) and end-stage renal disease (ERDS). From a metabolic perspective, lean patients with type 2 diabetes mellitus (T2DM) and renal disease might also benefit from SPK.

**Methods:** Data from all consecutive T1DM and T2DM patients who received a SPK transplant at the UKL were analyzed. T2DM patients receiving a kidney transplant alone (KTA) served as control. Donor, recipients- and long-term-, endocrine, metabolic and graft outcomes were compared among all groups investigated.

**Results:** Eighty-nine T1DM and twelve T2DM patients received a SPK and twenty-six T2DM patients were transplanted with a KTA. Patient survival at 1 and 5 years: T1DM: 89.9% and 88.8%, T2DM: 91.7% and 83.3% and T2DM KTA: 92.3% and 69.2% ( $p = 0.002$ ). Pancreas graft survival for SPK at 1 and 5 years was: T1DM: 83.1% and 78.7% and T2DM: 91.7% and 83.3% ( $p = 0.712$ ). Kidney graft survival at 1 and 5 years was T1DM: 88.8% and 79.8% and T2DM: 91.0% and 83.3% and T2DM KTA: 80.8% and 65.4% ( $p < 0.001$ ). Delayed graft function (DGF) rate was significantly higher in type 2 diabetics receiving a KTA. Surgical, immunological and infectious complications showed similar results for all groups. Mean triglyceride level was significantly lower in T1DM recipients compared to T2DM before transplantation ( $p = 0.042$ ) and mean high-density lipoprotein (HDL) – cholesterol levels were significantly higher in T1DM recipients, when compared to T2DM patients before transplantation ( $p = 0.015$ ). Lipid profiles remained significantly altered over a period of 5 years after transplantation ( $p = 0.04$ ).

**Conclusion:** With regard to metabolic function a selected group of patients with T2DM benefit from SPK transplantation. Consensus and limitations for SPK transplant indications in T2DM patients are warranted.

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### LABORATORY BIOMARKERS IN THE PREDICTION OF CARDIOVASCULAR RISK AFTER KIDNEY TRANSPLANTATION

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**Background:** Chronic kidney disease and kidney transplantation (KT) are associated with an increased cardiovascular risk. Therefore, KT recipients are subjected to a careful pre-transplant check-up and regular ambulatory visits with concomitant laboratory controls. We performed a retrospective evaluation of laboratory biomarkers routinely controlled before and after KT to identify those bearing a predictive value in cardiovascular outcome.

**Methods:** In a retrospective chart review, adult KT recipients (n = 504) between 2003 and 2014 from our center were evaluated. Besides baseline clinical and demographical characteristics, we recorded the rate of post-transplant major adverse cardiac events (MACE), a composite of all-cause mortality, acute coronary syndrome, stroke and heart failure within 2 years after KT. In four given time points – at the time point of wait-listing for KT as well as at the 6, 52 and 104 week after KT respectively – following laboratory parameters were recorded: complete blood count, CRP, kidney function parameters, HbA1c, iPTH, lipids and hs-troponin T in serum as well as albumin in serum and urine. Statistical significance of the differences was tested using Mann-Whitney-U or Kruskal-Wallis tests,  $p < 0.05$  was considered significant.

**Results:** As expected, serum creatinine showed a marked decline after KT, whereas HbA1c tententially increased over time, but remaining in a non-pathological range. The occurrence of post-transplant MACE was 8.7% (n = 44). Patients without MACE had a significantly lower hs-troponin T prior to KT. Patients with MACE were characterized by worse kidney function and higher CRP levels. MACE occurrence was associated with greater albuminuria and significantly higher iPTH in serum after 1 year following KT.

**Conclusions:** Apart from established cardiovascular risk predictors (e.g.: kidney function, albuminuria), higher iPTH levels after 1 year were associated with worse cardiovascular outcomes following KT. The significance of this observation is limited by the retrospective character of the study as well as low MACE count.

## BASIC SCIENCE

## 049 ROLE OF MHC VERSUS MINOR MISMATCHES IN IL-2/ANTI-IL-2 COMPLEX INDUCED SKIN GRAFT SURVIVAL

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**Background:** Interleukin-2 (IL-2) coupled to a specific antibody against IL-2 (IL-2 complexes) has shown to selectively expand and activate Tregs in vivo. Utilizing this approach induction of tolerance towards islet allografts was already shown. However, only little success could be achieved in a fully mismatched skin transplantation setting. Here we investigate the mechanisms leading to prolonged skin graft survival in different strains and the role of MHC versus minor antigens.

**Methods:** Recipient mice (C57BL/6) received fully mismatched BALB/c, C3H or minor mismatched BALB/b skin grafts in combination with IL-2 complexes (1  $\mu$ g IL-2/5  $\mu$ g JES6-1), Rapamycin (Rapa; 1 mg/kg; i.p.) and a short-term treatment of anti-IL-6 mAb (300  $\mu$ g i.v.). To study the mechanisms of tolerance, development of donor-specific antibodies was investigated and flow cytometric analyses for evaluation of specific leucocyte subpopulations were performed. In addition, groups of mice were depleted of CD8+ cells using an anti-CD8 antibody (0.5 mg i.p.; d-3 and d-1) in order to study the involvement of this leucocyte subset on allograft survival.

**Results:** We set out show that the combination of IL-2 complexes with Rapamycin and an IL-6 neutralizing antibody leads to significantly prolonged survival of fully mismatched skin allografts (MST = 29 days;  $p < 0.0001$ ), which is even more extended within the minor mismatch model (MST = 60 days;  $p < 0.0001$ ). Furthermore, analyses of sera showed a complete absence of donor reactive IgG. For CD8+ cell depletion, no further prolongation of allograft survival was observed, suggesting a minor role of these cells within acute rejection if IL-2 complexes, Rapamycin and anti-IL-6 mAb were administered.

**Conclusion:** The combined treatment of IL-2 complexes, Rapamycin and anti-IL-6 mAb leads to significantly prolonged fully or minor mismatched skin graft survival and prevention of donor-reactive antibody production. However, the mechanisms and cell subpopulations responsible for late graft loss are still not fully understood and therefore, further experiments are warranted.

## 050 IL-2-COMPLEX TREATMENT AND THE EFFECT ON THE B CELL COMPARTMENT

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**Introduction:** Treatment with IL-2-Complexes (IL-2-cplx) allows the selective expansion of regulatory T cells (Tregs) and has been demonstrated to impair allograft rejection with the complete absence of donor-specific antibodies (DSA). Here, we focused on the effect of IL-2-cplx treatment on B-cells and changes in the expression of markers relevant for immune response activation.

**Methods:** C57BL/6 mice received intraperitoneal injections of either PBS (control) or IL-2-cplx (1  $\mu$ g IL-2/5  $\mu$ g anti-IL-2) for five consecutive days and were sacrificed on day 7. In selected groups, Tregs were depleted with anti-CD25 mAb. We used state of the art 12 color flow-cytometric analysis to investigate the frequency of T- and B-cell subpopulations with focus on the expression of MHC-II and important costimulatory molecules for B-cell immune response, namely CD80, CD86, and PDL-1 in lymphoid tissues.

**Results:** Beside a significant increase in Tregs (19.4% vs 4.2%,  $p < 0.001$  in spleen; 13.5% vs 5.9%,  $p = 0.03$  in lymph nodes; vs naive) treatment with IL-2-cplx resulted in elevated numbers of plasma cells (PC) (1.57% vs 0.44%,  $p = 0.03$ ). Moreover, Treg depletion led to a decrease in PCs (2.20% vs 0.64%,  $p = 0.07$ ). Administration of IL-2-cplx led to an increase of germinal center (GC) B-cells (0.72% vs 0.53%,  $p = 0.01$ ) and a decrease of Bcl-6 expression in GC B-cells (30.3% vs 16.8%,  $p = 0.01$ ; vs naive). Additionally, IL-2-cplx treatment significantly enhanced the surface expression of MHC-II (MFI = 109326 vs 79233,  $p < 0.001$ ) and PDL-1 (MFI = 7026 vs 5010,  $p = 0.001$ ) on B-cells compared to naive mice.

**Conclusion:** The present findings demonstrate an important role for Treg cells in B cell biology that may have further implications in immune cell modulation protocols for human organ transplantation. Further research to explore the mechanism between PCs and Tregs are warranted.

## 051 TISSUE AND SUBSET-SPECIFIC EFFICACY OF ATG MEDIATED T-CELL DEPLETION IN EXPERIMENTAL MURINE HEART TRANSPLANTATION

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**Background:** Anti-thymocyte-globuline (ATG) provides profound T-cell depletion and is commonly used as induction therapy in transplant recipients. However, ATG preparations are not standardized and vary substantially between manufacturers. Furthermore, adequate preparations for use in mice are rare and subsequently little is known about their lineage-specific efficacy. We therefore sought to investigate rabbit anti-mouse rATG (Thymoglobulin) in our mouse model for murine heart transplantation.

**Methods:** Naive wildtype C57BL/6 mice were injected intraperitoneally with rabbit anti-mouse rATG (Thymoglobulin, provided by Sanofi), in a very high dose (VHD: 0.5 mg/injection), a high dose (HD: 0.25 mg/injection) and a low dose (LD: 0.15 mg/injection) regimen on days 0 and 5. Flow cytometry was performed on days 3 and 8 to assess depletion within major compartments (blood, spleen, lymph nodes, thymus and bone marrow) and across relevant lymphocyte subpopulations.

**Results:** ATG demonstrated profound T-cell depletion with a more than 95% reduction in the frequency of CD3+ positive cells in peripheral blood on day 8. We observed no significant difference in the degree of depletion on day 8 between the three dosages. CD8+ T-cells were affected to a greater extent (>99% reduction) than CD4+ T-cells (90% reduction). In contrast, regulatory T-cells (Tregs) were relatively spared by ATG, causing elevated Treg frequencies up to 17% of CD4+ T-cells compared to 7% in untreated mice ( $p < 0.05$ ) in peripheral blood. Similar depletion-patterns were observed in secondary lymphoid organs (spleen and lymph nodes). In contrast, within the thymus no depletion of mature T-cells or progenitors was detected. Memory T-cells overall showed less depletion than naive ones. In spleens and lymph nodes, the effector-memory T-cell subpopulation (T<sub>EM</sub>) was affected the least by ATG.

**Conclusion:** Rabbit anti-mouse ATG provides thorough T-cell depletion in peripheral blood and secondary lymphoid organs. The depleting effect of ATG varies across T-cell subpopulations, relatively sparing memory and regulatory T cells while profoundly depleting naive T-cells. Strikingly, ATG does not deplete intrathymic T cells even at high doses, warranting future investigation of preserved intrathymic alloreactivity after ATG therapy.

## 052 NATURAL KILLER CELLS PROMOTE KIDNEY GRAFT REJECTION INDEPENDENTLY OF CYCLOSPORINE A THERAPY

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**Background:** Natural Killer (NK) cells have recently been recognized as key players in antibody-mediated chronic allograft failure, thus requiring a

comprehensive understanding in order to address whether NK cells can escape conventional immunosuppressive regimens.

**Methods:** Influence of cyclosporine A (CyA) on NK cell function was studied in a mouse model of allogeneic kidney transplantation (KTX, BALB/c to C57BL/6). Recipients were treated daily with CyA (10 mg/kg) for seven and 14 days (day 56).

**Results:** Administration of CyA in recipients resulted in significantly reduced frequencies of intragraft CD4<sup>+</sup> and CD8<sup>+</sup> T cells, illustrating a reduced capacity of IFN $\gamma$  production. In contrast, NK cell frequencies remained unaffected in CyA recipients and IFN $\gamma$  production and cytotoxicity of NK cells were not reduced as compared with controls. Importantly, the additional depletion of NK cells in combination with CyA resulted in a further improvement in kidney function until day 7 and prolonged overall graft survival until day 56 as compared to the untreated controls. Surviving animals demonstrated higher intragraft frequencies of CD4<sup>+</sup>FoxP3<sup>+</sup>Ki67<sup>+</sup> regulatory T (T<sub>REG</sub>) cells as well as higher frequencies of CD8<sup>+</sup>CD122<sup>+</sup>T<sub>REG</sub>.

**Conclusion:** We here demonstrate for the first time that NK cell depletion combined with CyA synergistically improves graft function and prolongs graft survival, suggesting that NK cell targeting constitutes a novel approach for improving KTX outcomes.

**053 SIMVASTATIN DONOR THERAPY NEGATIVELY INFLUENCES CELL VIABILITY IN A MURINE HEART TRANSPLANTATION MODEL**

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**Background:** Simvastatin (SV) is an established therapeutic agent applied in primary and secondary prevention of cardiovascular diseases due to its lipid-lowering effect. However, several "pleiotropic" effects including antioxidant properties are still under investigation. The aim of this study was to investigate if a single donor SV treatment prevents from ischemia reperfusion injury (IRI) induced graft damage in a murine heart transplantation model.

**Methods:** In a syngeneic murine heart transplantation model, male C57Bl6 wild type mice were used as size-matched donor recipient pairs. Donors were either pretreated with a single oral dose of 20 mg/kg b.w. simvastatin or remained untreated. Grafts were exposed to 9 h cold ischemia time (CIT). Following 2, 12 or 24 h reperfusion, graft heart beating score was monitored and cell viability was assessed by confocal microscopy. Histomorphological changes were examined in H&E stained tissue. Mitochondrial stress was assessed by cardiolipin HPLC-MS.

**Results:** In comparison to untreated grafts, 2 h reperfusion resulted in a markedly reduced heartbeating score in SV-treated grafts (p = ns). While this difference disappeared following 24 h reperfusion, confocal microscopy revealed a statistically significant reduction in cell viability following 2 h as well as 24 h reperfusion in SV-treated grafts, when compared to respective controls (p = 0.024, p = 0.03, respectively). Additionally, mitochondrial stress was present in all transplanted grafts independently from pretreatment.

**Conclusions:** Simvastatin donor treatment leads to a reduction in cell viability and is unable to prevent from IRI-associated graft in the applied murine heart transplantation model.

**054 THE ROLE OF MATURE AND IMMATURE DENDRITIC CELLS IN VCA COMPARED TO SOLID ORGAN AND SKIN TRANSPLANTS**

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**Background:** Cell-based therapies in vascularized composite tissue allotransplantation (VCA) have demonstrated promising results with the potential to modify life-long conventional immunosuppression. Dendritic cells (DCs)

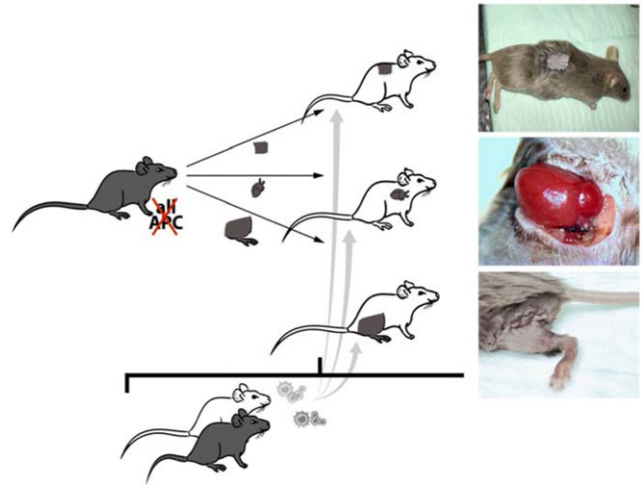
promote pro-inflammatory and alloimmune responses. Of particular interest is the role of DCs as antigen-presenting cells and potential tolerogenic effects as immature DCs.

**Material and Methods:** Diptheria Toxin Receptor (DTR) transgenic donor mice (zDC-DTR and CD207-DTR) were used to deplete subsets of DCs or LCs in a fully histoincompatible murine hind limb, heart (SOT) and skin transplant models; and were treated with DT 15 h prior to Tx; DBA/2J mice served as recipients (Fig. 1). Groups were divided into depletion protocols with DT treatment only; DT treatment with injection of either donor- or recipient derived immature DCs, and wild-type (WT) controls. Transplant recipients went through an observation period of 6 days. Alloimmune response was assessed sequentially; graft survival, intragraft structural and inflammatory changes were tested via immune analyses.

**Results:** Activated and matured DCs (CD11c+/CD40+, CD11c+/MHCII+) as well as Th17 cells (CD4+/IL17A+) were significantly increased in WT (C57BL/6J) controls; activated/matured DCs and Th17 cells had significantly decreased in depletion only (zDC-DTR and CD207), depletion + iDC/donor and depletion + iDC/recipients (p < 0.001 all groups). Tregs (CD4+/CD25+/Helios+) and B cells, had decreased in recipients with grafts from DTR mice (p < 0.01 respectively). We observed organ-specific immune responses: hind limb and heart transplant recipients demonstrated comparable rejection kinetics and intragraft changes. In contrast, immune responses following skin transplants were increased. CD11c+ DCs counts in skin transplants were significantly elevated.

**Conclusion:** This is to our knowledge the first systematic study of mature and immature DCs tested across VCA, SOT, and skin transplants. Those data may help explaining split-tolerance phenomenon in VCA while providing a basic concept for the utilization of mature and immature DCs in modifying alloimmune responses in VCA transplants.

Figure 1



**EXTRACORPOREAL PHOTOPHERESIS**

**055 EXTRACORPOREAL PHOTOPHERESIS IMMEDIATELY AFTER HEART TRANSPLANTATION IN HIGH-RISK PATIENTS**

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**Introduction:** Extracorporeal photopheresis (ECP) is an established therapy for treatment of heart transplant rejection and is also applied for rejection prevention in the perioperative setting after heart transplantation (HTX). Recently, we started a new protocol with avoidance of antibody induction therapy and calcineurin inhibitor (CNI) delay in high-risk patients after HTX incorporating ECP as rejection prophylaxis.

**Methods:** We report our first experience on 16 patients that were treated according to this protocol. Inclusion criteria were: history of cancer (n = 4), bridge to transplant via extracorporeal membrane oxygenation (ECMO) (n = 4) and eight patients had infections within 1 month before HTX. None of the patients received antithymocyte globuline (ATG) as induction therapy. Immunosuppression consisted of low-dose tacrolimus (target range 7–10 ng/mL in month 1–3, 5–10 ng/mL >3 months) with a delayed start (2–7 days post HTX) mycophenolate mofetil (MMF: 2 mg/day), and steroids (0.2 mg/kg starting on day 7, tapering to 0.03 mg/kg until end of first year). ECP was applied according to the protocol published by M. Barr (NEJM 1998) on days 2 + 3, 5 + 6, 10 + 11, 17 + 18, 27 + 28, 2 times every other week for months 2 and 3, and 2 times every 4 weeks at months 4–6 after HTX. Routine biopsy protocol was performed in weeks 2, 3, 4, Months 2, 3, 6 and 12 and whenever, there were clinical signs of acute rejection.



**Results:** Fifteen of 16 (82%) patients are alive with excellent graft function after a median follow-up of 8.3 (range, 0.25–33) months after HTX. Two patients showed biopsy proven signs of cellular rejection. One patient (2R rejection according to histology) was treated with steroids and in another patient with (1R) immunosuppression was switched from MMF to Ev. No signs of antibody-mediated rejection (ABMR) with C4d or C3d positivity were found in regular biopsies. Two patients developed severe pneumonia and one fever of unknown origin. One patient experienced candida septicemia but had candida positive skin swabs at the ECMO cannula insertion region pre-transplant. The latter patient died 1 week after HTX due to multi organ failure. One patient with history of cancer showed recurrence of disease and died 12 months after transplantation due to disease progression.

**Conclusion:** Up to now this is the first report on prophylactic ECP with avoidance of induction therapy and CNL delay in HTX patients. Infectious complications remain a problem in this high-risk group and occur in approximately 24%. However, ECP is a safe and effective strategy for patients at risk for cancer recurrence or sepsis to avoid organ rejection.

#### 056 EXTRACORPOREAL PHOTOPHERESIS AS INNOVATIVE TREATMENT FOR ANTIBODY-MEDIATED REJECTION

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**Background:** Within the last years, increasing attention has been given to the diagnosis and treatment of antibody-mediated rejection (AMR) due to its poor long-term outcomes. The therapeutic effect of extracorporeal photopheresis (ECP) on AMR is currently unclear. This study aimed to analyze the potential of ECP as adjunct treatment of AMR.

**Methods:** Our database was screened for patients who developed antibody-mediated rejection and were treated with extracorporeal photopheresis. The following parameters were evaluated: donor-specific antibodies, C4d deposition and lung histology.

**Results:** In total 38 patients developed AMR during follow-up. Among them 16 (42%) patients were treated only with immunoadsorption, 14 (37%) patients were treated with immunoadsorption followed by ECP, 3 (8%) with intravenous immunoglobulins and immunoadsorption and 5 (13%) patients with different treatments. Median time to AMR was 194 days (2–2380). Among the patients treated with ECP, thirteen had de novo donor-specific antibodies (DSA). Two of them had positive C4d staining and eleven of them showed signs of capillaritis or neutrophilic septal margination. ECP treatment was started after immunoadsorption and performed once a month for a minimum of 6 months. Median length of treatment was 12 months. In all patients treated with immunoadsorption followed by ECP, DSA disappeared or reduced under MFI threshold of 5000. No adverse events related to ECP were reported in any of the patients.

**Conclusions:** Extracorporeal photopheresis is associated with a reduction of de novo donor-specific antibodies during antibody-mediated rejection. Further studies are necessary to confirm its beneficial effect in this field.

#### 057 SUCCESSFUL USE OF EXTRACORPOREAL PHOTOPHERESIS AS THERAPY FOR ANTIBODY-MEDIATED REJECTION

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**Background:** Antibody-mediated rejection (AMR) gained attention in the last years due to its poor long-term outcomes. Unfortunately effective treatments are still missing and several therapeutic strategies are used by different centers. Herein we present a case of a lung recipient successfully treated with extracorporeal photopheresis.

**Clinical case:** The patient M.R. received in September 2015 a bilateral lung transplantation for idiopathic pulmonary fibrosis. No pretransplant donor-specific antibodies were detected back then. The patient received alemtuzumab induction therapy and a double immunosuppression protocol based on tacrolimus and cortisone. In April 2016, the patient presented at the outpatient clinic with dyspnea. A chest CT scan showed bilateral diffuse ground glass opacities. In the transbronchial biopsy a diffuse alveolar damage was diagnosed. C4d staining was negative and the histology did not show any capillaritis or neutrophilic infiltration. De novo donor specific antibodies of class I and II could be detected. With a diagnosis of probable AMR, the patient received 14 cycles of immunoadsorption in 3 weeks, showing clinical improvement. Since de novo DSA were still highly detectable, extracorporeal photopheresis was started as second-line treatment. Immediately after start of ECP, de novo DSA drastically reduced. The clinical situation of the patient improves further, the radiological investigations did not show any pathological findings and the patient still received ECP once every 6 weeks without showing signs of chronic rejection.

**Conclusions:** Extracorporeal photopheresis is associated with a reduction of de novo donor-specific antibodies and its potential as treatment of AMR should be investigated.

#### STEM CELL TRANSPLANTATION

#### 058 POSTTRANSPLANT OUTCOMES IN ALLOGENEIC AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN AUSTRIA IN COMPARISON TO THE EBMT BENCHMARK: A RETROSPECTIVE ANALYSIS OF THE AUSTRIAN SCT REGISTRY (ASCTR) 2000–2017

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**Background:** Recently, many changes have been made to improve the outcomes of hematopoietic stem cell transplantation (HSCT), including improvements in conditioning regimen, donor selection and prophylaxis, and in the treatment of organ complications, GVHD and infection. Although HSCT outcomes are gradually improving, they are still unsatisfactory. To determine the incidence, risk factors and post-SCT outcomes, we will conduct a retrospective population-based study among centers registered with the Austrian EBMT. The planned analysis of patients with acute myeloid leukemia (AML) and non-Hodgkin lymphoma (NHL) has a remarkable size, which is similar to landmark studies published by other registry groups. The benchmarking analysis will consider a series of risk factors that should be integrated into the statistical models to remove bias in the comparison of centres related to different patient population characteristics.

**Methods:** Evaluation of post-HSCT outcome of patients included into the Austrian EBMT registry; description of patients' characteristics and association with co-morbidities and other covariates; comparison of national EBMT analysis with other European countries and published data reported in peer-reviewed journals.

**Results:** The retrospective analysis is restricted to 1126 patients with AML, who underwent allogeneic HSCT and 1126 patients with NHL, who underwent autologous HSCT. The analysis refers to the period 2007–2017. Charts of the Austrian EBMT registry will be reviewed and data entries analysed. Descriptive and qualitative statistics will be applied.

**Conclusions:** Currently, country evaluations of the EBMT registry data are not reported in the published literature. The planned analysis provides unique real-world data from a large, complete, and unselected HSCT population. Results of allogeneic and autologous HSCT in Austria should be comparable within Austria as well as in regard to the EBMT benchmark by integrating a series of risk factors in the statistical outcome analyses according to the EBMT benchmarking model.

#### 059 HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SICKLE CELL DISEASE, EXPERIENCE OF THE PEDIATRIC TRANSPLANT CENTER IN GRAZ

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**Background:** Sickle cell disease (SCD) is a chronically progressive disease distributed worldwide, with high morbidity and mortality. Currently, red blood cell transfusions (exchange transfusions), hydroxyurea and concomitant supportive therapies are important disease-modifiers. Hematopoietic stem cell transplantation (HSCT) is curative, but often limited by a lack of available HLA-identical donors. Myeloablative, HLA-identical sibling transplantation in children with SCD offers excellent long-term survival. However, the risk of graft versus host disease (GVHD), infections, infertility, and other long-term transplant complications, limits its widespread use.

**Patients and Methods:** We report 6 patients transplanted in Graz using myeloablative conditioning and bone marrow (n = 3) or CD3 TCR alpha/beta CD19 depleted peripheral blood stem cells (PBSC) (n = 3) of matched family donors (n = 5) or a haploidentical family donor (n = 1).

**Results:** All patients tolerated the conditioning regimen and the transplant procedure very well. They showed a quick three lineage engraftment. Immunosuppression was based on Mycophenolate Mofetil (n = 5) or Cyclosporine A (n = 1). One patient suffered from chronic GVHD of liver and skin responding to extended multimodal immunosuppression including extracorporeal photopheresis. One patient presented mixed chimerism with a low percentage of donor derived T-cells (12%). The graft was rescued by application of two donor lymphocyte infusions. All other patients had a stable full-donor chimerism in WBC and sorted subtypes (B-cells, T-cells, Monocytes, NK-cells, Granulocytes).

**Conclusions:** HSCT for patients with severe SCD from an HLA-identical sibling offers an excellent 5-year survival. Improving transplant technologies such as modern graft manipulation techniques, combined with use of

haploidentical donors are promising and associated with reduced graft failure, incidence of GvHD and transplant related mortality. The outcome of the six presented patients proof the benefit of HSCT in children with SCD. However, long-term results of patients are necessary to further extent the awareness of the benefits of HSCT in patients with severe SCD.

060

#### FIRST PEDIATRIC DATA OF MANAGEMENT OF CMV REACTIVATION AFTER HSCT WITH LETERMIVIR

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**Background:** Letermovir is a new antiviral drug with exclusive activity against human Cytomegalovirus (CMV) and is licensed for CMV prophylaxis in adult HSCT recipients. Pediatric data are missing so far.

**Patients and Methods:** Five patients received 240–480 mg of letermovir adapted to bodyweight orally once daily (with no co-administration of cyclosporine A) after allogeneic HSCT following myeloablative conditioning. Two completed letermovir treatment, 3 patients still are receiving Letermovir.

**Results:** Both patients who completed Letermovir treatment became negative for CMV within 1 week (patient 1) and 3 weeks (patient 2), after initiation of letermovir, and remained negative for 3 months (patient 1) and 4 months (patient 2) respectively. In both patients, we observed rising liver parameters during letermovir treatment (AST, ALT and GGT in patient 1, and GGT and bilirubin in patient 2). In patient 1, hepatopathy turned out to represent histologically proven GvHD. In patient 2, hepatopathy was only mild and self-limiting. Both patients additionally received other hepatotoxic substances. Letermovir peak levels were within the ranges reported in adults receiving recommended dosages, while trough levels in our patients were higher than reported median trough levels in adult cohorts (1640–2190 versus 506.4–1201 ng/mL). The 4 remaining patients under ongoing Letermovir administration will be evaluated after completion.

**Conclusions:** Although our data are limited to only few pediatric patients with only a few letermovir plasma levels, we present first data on letermovir in the pediatric and therapeutic setting. As long as pharmacokinetic and safety data from pediatric patients are pending, dosages have to be chosen with caution. In conclusion, letermovir is promising, even as a therapeutic agent. More pediatric data including pharmacokinetic and safety data are urgently needed.

061

#### INTESTINAL ADENOVIRUS SHEDDING BEFORE ALLOGENEIC STEM CELL TRANSPLANTATION IS A RISK FACTOR FOR INVASIVE INFECTION POST-TRANSPLANT

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Human adenoviruses (HAdV) are a major cause of morbidity and mortality in pediatric human stem cell transplant (HSCT) recipients. Our previous studies identified the gastrointestinal tract as a pivotal site of HAdV persistence and reactivation, but the role of intestinal virus shedding pre-transplant for the risk of ensuing invasive infection has not been entirely elucidated. Molecular HAdV monitoring of serial stool samples using RQ-PCR was performed in 304 children undergoing allogeneic HSCT. Analysis of stool and peripheral blood specimens was performed pre-transplant and at short intervals until day 100 post-HSCT. The virus was detected in stool samples of 129/304 (42%) patients, and 42/129 (33%) tested positive already before HSCT. Patients displaying HAdV shedding pre-transplant showed a significantly earlier and more rapid increase of intestinal HAdV levels above the critical threshold of 10E6 virus copies/g stool ( $p < 0.01$ ) associated with high risk of invasive infection. In this subset of patients, critically high virus titers in stool appeared already within the first 3 weeks post-HSCT, and the occurrence of invasive infection characterized by viremia was significantly higher than in patients without HAdV shedding before HSCT (33% vs 7%;  $p < 0.0001$ ). The data demonstrate that intestinal HAdV shedding before HSCT confers a greatly increased risk for invasive infection and disseminated disease post-transplant, and highlights the need for early HAdV monitoring and pre-emptive therapeutic considerations in HSCT-recipients.

062

#### TORQUETENOVIRUS DYNAMICS AND IMMUNE MARKER PROPERTIES IN PATIENTS FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A PROSPECTIVE LONGITUDINAL STUDY

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Torquetenovirus (TTV) has been proposed as a marker of immune function in patients receiving immunosuppression after solid organ transplantation. This study aimed to define TTV plasma dynamics and investigate clinical associations in patients following allogeneic hematopoietic stem cell transplantation (HSCT). This was a single-center prospective longitudinal study involving 50 consecutive patients treated with HSCT between March 2015 and April 2016. TTV plasma DNA levels were measured with quantitative PCR at 12 consecutive time points during the first year after HSCT. Forty of the 50 patients (80%) had detectable TTV viremia before HSCT (median level, 5.37 log<sub>10</sub> copies/mL; interquartile range [IQR], 3.51–6.44 log<sub>10</sub> copies/mL). All patients subsequently developed TTV viremia during the follow-up period. Plasma viral loads evolved dynamically over time, with a peak of 8.32 log<sub>10</sub> copies/mL (IQR, 7.33–9.35 log<sub>10</sub> copies/mL) occurring at 79 days (IQR, 50–117 days) following HSCT and a stable plateau toward the end of the follow-up period. The type of malignancy, the use of antithymocyte globulin during conditioning, and the occurrence of acute graft-versus-host disease requiring systemic therapy had temporary effects on TTV dynamics. TTV levels showed a significant correlation with absolute lymphocyte counts following engraftment ( $r_s = -0.27$ ;  $p < 0.01$ ) and with cytomegalovirus (CMV;  $r_s = 0.39$ ;  $p < 0.01$ ) and Epstein-Barr virus (EBV;  $r_s = 0.45$ ;  $p = 0.02$ ) viral loads during phases of viremia. Immune-related clinical events were not predicted by TTV levels. TTV viremia occurred universally and was sustained throughout the first year after HSCT. Several variables and events before and after HSCT were correlated with TTV levels and hint toward immune marker properties of TTV, but their complex interactions might perturb the capability of TTV to predict immune-related complications in this population.

#### POSTERWALK I

063

#### LIVER TRANSPLANTATION FOR GIANT POLYCYSTIC LIVER

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**Background:** Polycystic liver disease with massive hepatomegaly can be an indication for liver transplantation (LT). Hepatectomy is a challenging procedure with difficult mobilization, risk for bleeding and the highest mortality rate among all causes for LT. Until now, there is no standard for safe hepatectomy described in the literature.

**Case Report:** A 34-year-old sarcopenic woman presented with both abdominal discomfort and dyspnea due to a huge belly circumference. The underlying giant polycystic liver diagnosed 13 years earlier made her almost immobile. The patient was listed for the today's standard piggy-back liver transplantation (pbLT). For pbLT inferior vena cava (IVC) preserving recipient hepatectomy is necessary. Since giant livers cannot be mobilized to get access to the IVC the deceased liver was split in half which is not a standard procedure during LT and then removed after total inflow control. The uneventful IVC preserving procedure for hepatectomy was performed with LigaSure<sup>®</sup>. The deceased liver weighed 17.5 kg. PbLT was performed subsequently. This is the first time to our knowledge that giant 17.5 kg polycystic liver was removed in an IVC-preserving manner for subsequent pbLT. At 6-months follow-up the patient presents in an excellent condition.

**Conclusion:** The large, rigid liver of patients with polycystic liver disease complicates hepatectomy. Dissection of the liver in the midline is a quick approach with limited blood loss and offers a safe procedure for hepatectomy.

064

**HEPATIC ARTERY RECONSTRUCTION UNDER THE MICROSCOPE IN PEDIATRIC LIVER TRANSPLANTATION – IS IT WORTH THE EFFORT?**

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**Introduction:** The incidence of hepatic artery thrombosis (HAT) after pediatric liver transplantation (PLT) is being described in up to 28.1%. Depending on the graft type, the hepatic artery (HA) diameter being anastomosed is very small. If thrombectomy is unsuccessful, retransplantation is the only option. We herein describe our experience with HA reconstruction under the microscope. **Methods:** Single center retrospective analysis of all pediatric liver transplantations (age <16 years) carried out between 01/2011 and 05/2019. Since 01/2015, in cases of living donation or left lateral or extended right splits with the artery cut at the level of the right/left HA, reconstruction is carried out under the microscope using 10/0 or 11/0 silk interrupted sutures. In all other cases HA reconstruction was either carried out using loops and 7-0/8-0 prolene running/interrupted sutures. 1-year graft and patient survival was assessed by Kaplan–Meier analysis. Primary endpoint was hepatic artery thrombosis.

**Results:** 51 PLTs – 12 living donor PLTs (23.5%, 11 left lateral segments, 1 left hemiliver) and 39 livers from brain dead donors (76.5%, 25 left lateral segments, 11 full size organs and 3 extended right grafts) have been carried out in the period observed. Overall 1 year survival was 92.16%. In 14 cases (27.45%), the HA was reconstructed under the microscope. HAT occurred in 0 patients (0%) in the microscope group and in 7 patients (18.92%) in the lupe group.

**Conclusion:** Based on our results we highly recommend hepatic artery reconstruction under the microscope.

065

**HIGHER PRE-TRANSPLANT KDIGO STAGES INCREASE THE RISK FOR EARLY GRAFT REJECTION EPISODES AFTER LIVER TRANSPLANTATION**

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**Background:** Compromised renal function prior to liver transplantation is a known risk factor for post-transplant patient survival which is especially relevant in MELD-based allocation systems. However, the impact of higher pre-transplant KDIGO stages on post-transplant rejection-free graft survival remains to be determined.

**Methods:** Patients with primary liver transplantation at Medical University Graz between the 1.1.2007 and the 31.12.2018 were included. Patients with additional kidney transplantation were excluded from analysis leading to a cohort of 211 patients for investigation of independent risk factors for rejection free graft survival using multivariable Cox regression analysis.

**Results:** Kaplan–Meier analysis demonstrated a significant influence of the number of rejection episodes on long-term patient survival ( $p < 0.001$ , log rank test). Multivariable Cox regression revealed that higher KDIGO stages increased the risk for early graft rejection independently and significantly in the long-term (HR = 1.273,  $p = 0.025$ ), whereas a D+/R– CMV mismatch was a protective factor for rejection-free graft survival (HR = 0.427,  $p = 0.027$ ). Low dose ATG induction (0.5–1.0 mg/kg/day for 3–4 days) did not have an influence on both study end-points.

**Conclusion:** ATG induction with higher dosages (>1.0 mg/kg/day for 3–4 days) may be able to reduce the increased risk for rejection-free graft survival in patients with higher pre-transplant KDIGO stages. D+/R– CMV mismatch reduces the risk of early rejection as has been reported before (Dogan et al., 2018).

**Reference:** 1. Dogan N, Hüsing-Kabar A, Schmidt HH, Cicinnati VR, Beckebaum S, Kabar I (2018). Acute allograft rejection in liver transplant recipients: Incidence, risk factors, treatment success, and impact on graft failure. *J Int Med Res.* 2018 Sep;46(9):3979–3990. <https://doi.org/10.1177/0300060518785543>. Epub 2018 Jul 12.

066

**NORMOTHERMIC MACHINE PERFUSION OF A RIGHT EXTENDED LIVER SPLIT: A CASE REPORT**

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**Background:** Normothermic machine perfusion (NMP) has been shown to be a safe preservation method of liver grafts and additionally to be of enormous logistic value. We herein present the first case of NMP and subsequent transplantation of an ex-situ right-extended liver split graft.

**Methods:** On Back-table a right-extended liver split from a 42-year-old donor liver was performed. While the left lateral split (LLS) was assigned for re-transplantation to a 4-month-old boy, the right-extended liver graft has been allocated to a surgically complex 50-year-old recipient for re-transplantation. Since both recipients were highly complex, simultaneous surgery was deemed unsuitable due to resources and qualified staff. Hence after the split was performed the dissection plane of the right-extended graft was closed with a running absorbable suture, vascular cannulation was performed and while the LLS was transplanted, NMP of the right split was initiated.

**Results:** Perfusion parameters were within normal range over the entire period. Lactate levels decreased from 105 to 8 mg/dL over 11 h and 43 min of NMP. pH-value remained within physiological limits after attribution of 10 mL sodium bicarbonate. Following 713 min of NMP-time and a total preservation period of 1250 min (537 min CIT) the graft was successfully reperfused. However, while immediate graft function was optimal (AST 57 U/L, Bilirubin 3.32 U/L, INR 1.2 on day 7) other surgical complications prolonged the postoperative course in this critically ill patient. The patient eventually recovered and was transferred to a rehabilitation center on day 49 after re-transplantation. In the 6 month follow up, the patient presented in good clinical conditions with no signs of further complications and good graft function. Except for an isolated drug-associated elevation of gGT, liver parameters ranged within normal limits.

**Conclusions:** NMP of split liver grafts is feasible and can convert the second split liver transplantation in a scheduled procedure.

067

**PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION – AS IT STANDS**

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**Background:** In 1997 the pediatric living donor liver transplantation program was successfully initiated at the Medical University Innsbruck. A reduction of waiting time and therefore minimizing the wait – list mortality are well known effects that come along with living donation. We aim to assess the outcome and complications after liver transplantation in this study.

**Methods:** A retrospective cohort analysis of pediatric patients (aged <18 years) who received a living donor liver transplant between October 1997 and June 2019 was conducted. All patients received either a left lateral or a full – left liver graft from a close relative (parent, grandparent). Survival analyses using Kaplan–Meier statistics were performed to obtain survival rates. Furthermore, we addressed complications that led to graft loss or death as part of a quality – improving management.

**Results:** A total of 56 living related pediatric liver transplantations were performed within the last 22 years. Graft loss occurred in six patients (10.7%). In all patients early after transplantation, caused by small for size syndrome, hepatic artery thrombosis or portal vein thrombosis. All received a split or full size high – urgency liver retransplant from a deceased donor within 2 weeks. Two patients died (3.6%) in our cohort. One died due to a multiorgan failure immediately after retransplantation and the other one due to the underlying disease afterwards. The 18-year patient and graft survival was 94.4% and 88.9%.

**Conclusions:** Our pediatric liver transplantation program has matured over the last two decades. We could achieve excellent patient and graft survival rates by an exceptional interdisciplinary peri – transplant teamwork. Each discipline constantly developed their advancements according to the international standard. Our outcomes match with international survival rates. Anticipating upcoming complications by detailed surgical planning and deliberately donor selection are key factors influencing the outcome.



068

**PORCINE DERMAL COLLAGEN FOR ABDOMINAL CLOSURE AFTER PEDIATRIC LIVER TRANSPLANTATION**

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**Background:** Primary abdominal wall closure (PC) after pediatric liver transplantation (pLT) can become challenging based on graft to recipient size mismatch and pre-existing abdominal wall defects due to previous surgeries. Herein we describe our experiences with the use of porcine dermal collagen graft (PDCG), as acellular graft for abdominal wall closure after pLT in patients <2 years.

**Materials and Methods:** Retrospective analysis for patients <2 years undergoing pLT between 01/2011 and 12/2014 was performed. Patients were divided into PC- and PDCG- groups. Primary endpoints were post-operative abdominal wall infections. Secondary endpoints included 1- and 5-year patient and graft survival (assessed by Kaplan Meier estimates) and development of abdominal wall hernia (T-Test).

**Results:** 15 out of 23 patients (65.2%) received a PDCG with a median of 22.7 (SD ± 11.0) days after pLT. Children receiving a PDCG did not have significantly more abdominal surgeries before LT (n = 1.0; SD ± 1.0) when compared to the control (n = 0.8; SD ± 1.1, p = ns). There was no difference in graft types within the two groups. A median of 3.3 (SD ± 1.9) surgeries after pLT took place prior to PDGC implantation and a median of 2.1 (SD ± 2.2) surgeries before final abdominal wall closure in the PC group (p = ns). One PDCG patch had to be removed due to infection (n = 1, 6.7%). Thrombotic events (hepatic artery thrombosis 23.1% vs. 14.3% and portal vein thrombosis 15.4% vs. 0%) occurred more frequent before definite closure in the PDCG-group when compared to PC. After pLT overall 1- and 5-year patient survival was 91.3% and 87.0% respectively. Abdominal wall hernias were observed in two patients of the PDCG group (25.0%) and none in the PC- group (0%; p = ns).

**Conclusion:** PDGC can be safely used for abdominal wall closure after liver transplantation in children <2 years of age.

069

**LIVER FUNCTION AFTER DUAL OXYGENATED HYPOTHERMIC EX VIVO LIVER PERFUSION PRIOR TO LIVER TRANSPLANTATION**

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**Background:** Organ preservation by machine perfusion has been recently implemented in clinical liver transplantation. Since May 2018, dual hypothermic liver perfusion (DHOPE) has been implemented in the clinical routine at our division. The aim of this study was to evaluate primary liver function after LT using perfused grafts.

**Methods:** Liver function parameters of 27 patients who received a hypothermic perfused graft was assessed and compared to 27 control patients, whose grafts were preserved by static cold storage and transplanted in the same time period. Perfused livers were connected to the Liver Assist Device and perfused at 10–14°C through the portal vein and hepatic artery, whilst being supplied with oxygen. No DCD livers were included in the study. Peak and 2-week levels of aspartate aminotransferase (ASAT), alanine-aminotransferase (ALAT), alkaline phosphatase (AP) and bilirubin were measured.

**Results:** In the first 90 days, 4 patients were lost in each group (HOPE group 1 PNF, 1 cardiac, 2 sepsis; control group 2 PNF, 2 sepsis). In the perfusion group, posttransplant peak levels (median (IQR)) reached: ASAT 1126 U/L (1606 U/L), ALAT 641 U/L (910 U/L), AP 116 U/L (91 U/L) and bilirubin 5.18 mg/dL (3.88 mg/dL). After 2 weeks a reduction of ASAT to 30 U/L (35.75 U/L), ALAT to 85 U/L (88.25 U/L) and bilirubin to 1.82 mg/dL (2.69 mg/dL) but an increase of AP to 137.5 U/L (130.75 U/L) was observed. The control group showed a trend towards higher peak levels of ASAT 1919 U/L (3045.5 U/L) (p-value = 0.101), ALAT 960 U/L (1752 U/L) (p-value = 0.0536), AP 128 U/L (115 U/L) (p-value = 0.395) and bilirubin 6.26 mg/dL (4.50 mg/dL) (p = 0.757). Two weeks after transplantation liver function parameters of the perfusion and control group were comparable.

**Conclusions:** This preliminary analysis shows that hypothermic perfusion of liver grafts is feasible and leads to similar early outcome compared to transplantation of static cold stored livers.

070

**ADULT, METACHRONOUS, ABO INCOMPATIBLE LIVING KIDNEY AND LIVER DONATION FROM THE SAME DONOR TO ONE RECIPIENT**

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With the presence of organ shortage, living donors remain important sources of grafts. At the same time a high demand for donor organs leads to the necessity of using living ABO incompatible (ABOi) donors. Metachronous living donor donation of two ABOi grafts from the same donor to one recipient has not been described before. Our experience of living kidney and liver transplantation in immunologically complex adult and pediatric recipients was the foundation for adapting to this procedure.

A 48-year old woman with Autosomal Dominant Polycystic Kidney and Liver Disease (ADPKD) received an ABOi kidney donation from her husband in 2014. Rituximab induction and preoperative plasmapheresis were necessary for ABOi transplantation. Both the donor and the recipient had an uneventful postoperative recovery. Maintenance immunosuppression consisted of Tacrolimus monotherapy after an initial course of tapered steroids. In 2017 the woman was listed for liver transplantation with a MELD score of 18. Again, her husband proved eligible for right lobe liver donation.

Recipient's donor specific HLA-Antibodies and Isoagglutinin Iso-Antibodies were negative pre-transplant. Preoperative extensive immunologic screening of both donor and recipient's myeloid and lymphatic systems suggested liver living transplantation without induction therapy followed by five prophylactic courses of plasmapheresis and iv-Immunglobulin therapy. Liver living transplantation was successfully performed late 2017. Maintenance immunosuppression was performed with MMF and Tacrolimus and tapered steroids. As an example, immunologic screening displayed a peri and immediate postoperative decrease in T regulatory cells. On postoperative day 5 T reg levels exceeded basic pre-transplant values (Figure 1). Immunosuppression was adjusted to Tacrolimus monotherapy accordingly to the immunologic follow-up screenings. Both donor and recipient had again and excellent postoperative course.

According to our knowledge this is the first report of adult metachronous ABO incompatible living kidney and liver donation from the same donor to one recipient. This procedure is feasible in a transplant center with advanced surgical and immunological expertise.

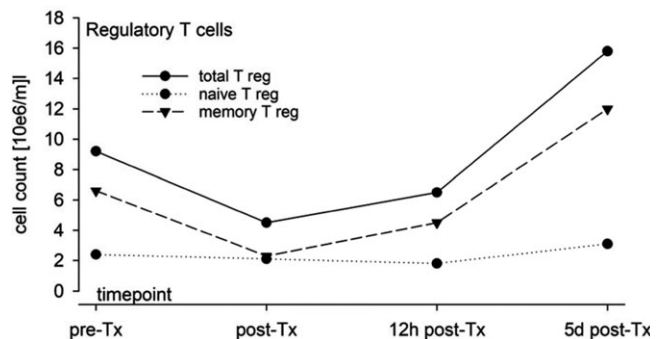


Figure 1. Pre- and Postoperative T regulatory cell values after ABOi liver transplantation in an ADPKD patient who already received an ABOi living kidney donation from the same donor 3 years earlier.

071

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

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

A systematic literature search for trials comparing generic vs. innovator Tac was conducted accordingly. A total of 17 controlled studies (5 LT, 11 KT, 1 LT/ KT) including 1413 patients were identified. 92.9% (13/14; 5/5 LT, 8/9 KT) of studies have reported same or lower BPAR with generics; however, only 33.3% (3/9; 1/2 LT, 2/7 KT) of (sub)studies show bioequivalence of generics according

to the area under the curve (AUC), 55.6% according to the concentration maximum ( $C_{max}$ ) (5/9; 2/2 LT, 3/7 KT).

The comprehensive review of 79 publications (21 LT, 58 KT) with a total of 30962 patients (5657 LT, 25305 KT) suggests cost effective generic Tac being comparable with innovator Tac in both clinically relevant and pharmacokinetic outcome data.

Data shown here provide clear evidence on the cost effective safe clinical use of generic Tac after both LT and KT.

### 072 AUTOLOGOUS RENAL TRANSPLANTATION FOR RETROPERITONEAL FIBROSIS: RETHINKING ORMOND'S DISEASE – A CASE REPORT

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**Background:** Retroperitoneal fibrosis (RPF, Ormond's disease) is a rare, chronic inflammatory disease characterized by retroperitoneal proliferation of fibrous tissue. The disease frequently results in ureteral obstruction, multiple surgeries and finally renal failure. We herein report case managed successfully by autologous renal transplantation.

**Case Report:** A 62-year-old woman, with a complex surgical history was referred to our department. She had undergone left-side nephrectomy several years ago due to kidney atrophy and presented with a progressive kidney dysfunction of the remaining right kidney. Furthermore, the patient had previously undergone a partial right-sided ureteral resection with bladder elevation and "definite" percutaneous nephrostomy was performed, concomitant by recurrent septicemias due to renal infections. Following the strong wish of the patient to preserve the remaining kidney, an autologous renal transplantation was planned. The right kidney was removed and perfused with 300 mL HTK. Two arteries were conjoined and the graft was transplanted into the left iliac fossa using the standard technique for living donor kidney transplantation (warm ischemia time 2 min, cold ischemia time 2 h 31 min, anastomosis time 25 min). Postoperatively, after a maximum creatinine increase up to 2.7 mg/dL the kidney recovered within a few days. Currently, creatinine (0.85–0.89 mg/dL) is lower than before autologous transplantation (1.09–1.39 mg/dL). A superficial wound infection was managed conservatively. The patient was discharged on the 18th postoperative day in excellent clinical condition.

**Conclusion:** Autologous renal transplantation should be considered as a treatment option for patients with persistent ureteral obstruction caused by RPF, even in complex cases.

### 073 RISK FACTORS FOR LYMPHOCELE

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**Background:** According to the literature, the incidence of lymphocele after renal transplantation is around 2–30%. There are several known risk factors, and we focused now on the repeated transplantations.

**Methods:** Based on the clinical history of two patients we reviewed our database.

**Results:** The majority of perinephritic fluid collections occurs immediately after the operation, during the first months. Late occurring lymphoceles are very rare. By leaving the postoperative drainage longer, most of these are treated in a conservative manner. Some more cases need a radiological postoperative drainage, the use of povidone-iodine can be beneficial. A small minority may require a surgical solution which means fenestration with omentoplasty either laparoscopically or open.

**Conclusions:** The risk of the development of lymphocele after kidney transplantation in the setting of repeated transplantations is increased.

### 074 VASCULAR SURGERY SKILLS IN CONNECTION WITH KIDNEY TRANSPLANTATIONS

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**Background:** Our intention was to investigate if vascular surgery skills are required in the context of kidney transplantation.

**Methods:** We performed a retrospective analysis including 332 kidney transplantations between 2010 and 2015 regarding arterial and venous

reconstructions as well as operative and radiologic -interventional revisions.

**Results:** In an analysis of 332 kidney transplantations of the last 6 years (including 95 living donor transplantations) in numerous cases the necessity of vascular surgery expertise could be shown. In 5.1% of the cases it was necessary to perform a thrombo-endarterectomy of the external iliac artery more extended than the length of the anastomosis. Only once an interposition of PTFE was required. At 54 kidneys (20%) an accessory kidney artery could be seen, at almost the half (46%) a re-anastomosis or creation of a common patch was done. Because of the needed length of the kidney vein in 74 cases (21%) a vena cava conduit was constructed with the existing vena cava. A postoperative revision was necessary in 37 cases (11%), in which the greater part was an evacuation of a hematoma. Only two times the anastomosis of the ureter was the reason of revision. One time only a great saphenous vein interposition at the renal artery was performed during the revision. Also in one case due to a lesion of the intima a plaque occluded the kidney artery, which was solved by thrombo-endarterectomy. Both situations were detected by obligatory postoperative colour coded duplex ultrasonography. An intraoperative reperfusion with Custodiol was needed in one case because of runoff obstruction based on a venous valve of the external iliac vein.

**Conclusions:** Our critical retrospective datas show that the expertise of a vascular surgeon performing kidney transplantations is useful because of the technical venous and arterial reconstructions.

### 075 CHALLENGES IN THE MANAGEMENT OF TWO VERY SMALL KIDNEYS FOR TRANSPLANTATION

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**Background:** For a 69 years old man there were two very small kidneys from a 73 years old female donor with 43 kg and a height of 153 cm offered. Both kidneys together had a total weight of 210 g. In the explanation form was mentioned that both kidneys had a cc-diameter less than 5 cm.

**Case Presentation:** After we got the permission from Eurotransplant to implant both kidneys in one recipient we performed the transplantation in the right extraperitoneal fossa iliacal. Therefore we decided to construct the kidneys at the back table and sutured both kidneys together. We made an anastomosis for the arteries as well as for the veins, so we got one common trunk for each vessel. After that we built an anastomosis with the iliacal vein first and second an anastomosis with the iliacal artery. For the urine flow we sutured both ureters together in the proper sense of an end to side anastomosis, protected by two double-J catheters and so we ensured a drainage of both kidneys to the urinary bladder.

**Conclusion:** Identifying and reporting of very small and less weight kidneys is essential. We could show that it is possible but challenging to transplant both kidneys in the extraperitoneal space on one patient side.

## POSTERWALK II

### 076 FEMALE RECIPIENT GENDER DETERMINES ADVERSE OUTCOMES FOLLOWING EXPERIMENTAL HEART TRANSPLANTATION

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**Background:** Clinical as well as experimental data on gender issues in solid organ transplantation remain scarce. However, recent observations indicate that recipient-donor gender mismatch could negatively impact allograft function post-transplantation.

**Methods:** Aiming to investigate clinically made observations in an experimental setting, male fully allogeneic Balb/c donor hearts were transplanted to either female (HTx-F) or male (HTx-M) C57BL/6 recipients in an acute and a chronic model.

**Results:** Applying an acute model without immunosuppression, grafts from female recipients revealed a significantly elevated expression of proinflammatory markers such as IL-2 ( $p < 0.01$ ) and IFN- $\gamma$  ( $p < 0.05$ ) on day 5 following transplantation. Simultaneously, IFN- $\gamma$  was upregulated in the spleen ( $p < 0.001$ ), indicating an elevated systemic inflammatory response compared to male controls (HTx-M). In addition, the disadvantageous effect of gender mismatch was even more pronounced in a chronic model (CTLA4-Ig

co-stimulation blockade), when transplantation of male hearts into female recipients resulted in a significantly shortened median allograft survival (HTX-F: 29 days vs. HTX-M: 50 days;  $p = 0.004$ ).

**Conclusion:** Our observations of inferior outcomes in female recipients foster the notion that gender disparities need to be crucially more highlighted in future solid organ transplant medicine.

#### 077 UPDATE ON DE NOVO SOLID ORGAN MALIGNANCIES AFTER LUNG TRANSPLANTATION

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**Background:** Lung transplant patients have an increased risk of de novo cancer due to long-term immunosuppression. A previous retrospective evaluation of the time period 1989 until 2014 revealed 55 solid organ malignancies (SOM) in 54 patients, corresponding to 3.6% of all 1491 transplanted patients. Since, immunosuppressive protocols have changed over time we sought to update this analysis.

**Methods:** This retrospective study included all patients who received double or single lung transplantation (LuTx) between 1989 and June 2019 at the Division of Thoracic Surgery at the Medical University Vienna. All relevant data were retrieved from the institutional database.

**Results:** In total, 72 patients of 1928 lung transplant recipients developed 75 SOM (3.7%). Patient characteristics were as follows: age at LuTx was  $51.5 \pm 13.3$  years, age at SOM diagnosis was  $55.6 \pm 14.1$  years, sex (male/female) 43/29, underlying disease for LuTx (COPD/fibrosis/CF/pulmonary hypertension/others) was 36 (50%)/15 (20.8)/7 (9.7%)/2 (2.8%)/12 (16.8%). Type of LuTx (double/single) was 49/13. Type of SOM were as follows: bronchogenic 23, digestive 27, urogenital 14, others (breast 5, head & neck 3). The mean time to from transplantation to diagnosis of SOM was  $1801 \pm 1393$  days.

**Conclusion:** The overall prognosis in patients with post-lung transplantation solid organ tumors is poor. Therefore, a careful and precise surveillance for high-risk patients is recommend detecting solid organ tumor in an early stage to improve the prognosis.

#### 078 THE USE OF POLYTRAUMA DONOR ORGANS DOES NOT IMPAIR LONG-TERM OUTCOME AFTER LUNG TRANSPLANTATION

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**Background:** Organs from polytrauma donors are often reported to be associated with impaired results in lung transplantation. Therefore, radiological signs of lung contusions are a reason for many centers to reject an organ offer outright. As a consequence, potentially viable organs are lost for the donor pool.

**Methods:** In a retrospective data analysis, we included a total of 751 patients who received standard double lung transplantation between January 2010 and June 2018 in our institution. All 102 patients transplanted using lungs from polytrauma donors were further divided into two groups: Group I ( $n = 46$ ) included polytrauma donors who had radiological signs of lung contusion; Group II ( $n = 56$ ) donors died from polytrauma but had a normal chest radiography. A total of 649 transplantations with non-trauma donors were assigned to Group III as a control. We compared short- and long-term outcomes of these three groups.

**Results:** In all three groups, basic demographic data and preoperative factors of the recipients were comparable. Median age of donors in group III was significantly higher with 44 years compared to 22 in group I and 36 years in group II, respectively. ( $p < 0.001$ ). Significant secretions in donor bronchoscopy were found more often in Group I (47.6%) compared to the other groups ( $p = 0.012$ ). Arterial  $pO_2$  and  $pCO_2$  at 100%  $FiO_2$  were comparable in the donors of all groups ( $p = 0.504$ ), as was pre-explant duration of mechanical ventilation ( $p = 0.729$ ). Recipients after transplantation showed similar rates of PGD 3 in all three groups (t24: 0.0% vs 0.0% vs 2.9%,  $p = 0.241$ ; t48: 2.3% vs 0.0% vs 3.0%,  $p = 0.438$ ; t72: 0.0% vs 0.0% vs 2.9%,  $p = 0.246$ ). Median length of ventilation was comparable with 45 (IQR 54) vs 34 (IQR 53) vs 41 (IQR 69) hours ( $p = 0.374$ ). In addition, long-term survival did not appear reduced in the two groups with polytrauma donors (5 years: 78.7% vs 89.0% vs 75.1%,  $p = 0.197$ ).

**Conclusion:** Donor organs after polytrauma lead to comparable short- and long-term results compared to non-trauma donors. Presence or absence of signs of lung contusion in chest radiographs or computed tomography did not show an impact on primary graft function and survival.

#### 079 QUALITY PARAMETERS OF DONOR LUNGS ACCEPTED FOR TRANSPLANTATION, DECLINED AT OFFER AND REJECTED AT TABLE

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**Background:** The donor evaluation form provided by Eurotransplant (ET) is a guide aiming to adequately judge the donor lung quality. However, the true quality of a donor lung is sometimes – even for experienced transplant surgeons – difficult to judge and often lungs, which look borderline on paper, are in fact transplantable with a good long-term outcome. This study aimed to analyze whether lungs accepted for transplantation, lungs rejected after retrieval and lungs rejected upon offer due to quality reasons differ in parameters provided by the ET donor report.

**Methods:** This retrospective single center study included all donors offered to the Lung Transplant Program Vienna between 2010 and 2018. Donor data provided by Eurotransplant (ET) were collected including blood group, donor type, gender, cause of death, smoking status, bronchoscopy findings, partial pressure ( $pO_2$ ,  $pCO_2$ ) and days of intubation.

**Results:** Of 2090 valid donor offers within the study period, 844 (40.4%) were successfully transplanted, 1502 (50.3%) were rejected at offer for quality reasons and 194 (9.3%) were retrieved and rejected at the table. The rate of non-heart beating donors amounted to 110 (5.9%), compared to 1761 (94.1) heart beating donors. Of the non-heart beating donors 78.2% were rejected upon offer, 2.7% rejected at the table and 19.1% transplanted. Most frequent causes of death were cerebrovascular incidents (69.5%), head trauma (11.6%) followed by poly trauma (7.3%). 40.4% of the overall donor population were smokers. Of those a significant rate (61.3%) was rejected at offer, 28.1% transplanted and 10.6% rejected at the table ( $p < 0.001$ ). Bronchoscopy abnormalities were reported in 430 offers. The majority of 71.2% was immediately rejected, 10% of the donor lungs were rejected at the table and 18.8% were transplanted.  $pO_2$  value was highest in organs used for transplantation (mean  $443.5 \text{ mmHg} \pm 100.2$ ). Lungs rejected upon offer had the poorest  $pO_2$  (mean  $357.5 \text{ mmHg} \pm 110.3$ ) and lungs rejected after retrieval had a mean  $pO_2$  of  $405.1 \text{ mmHg} \pm 109.4$ .  $pCO_2$  values did not differ between groups.

**Conclusion:** Lungs primarily rejected for quality reasons had worse blood gases and a higher likelihood of bronchoscopy abnormalities. Nevertheless, this study underlines the difficulties to adequately judge donor lung quality.

#### 080 THE IMPACT OF PROSPECTIVE HUMAN LEUKOCYTE ANTIGEN MATCHING IN PRE-SENSITIZED LUNG TRANSPLANT PATIENTS ON WAITING TIMES AND POST-TRANSPLANT OUTCOME

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**Background:** Pre-sensitized patients pose an increasing problem in contemporary lung transplantation. A possible strategy of managing these patients include pre- and post-transplant desensitization. However, in our center pre-sensitized patients are prospectively matched to confirm organ suitability. The aim of this study was to evaluate the outcome of such an approach.

**Methods:** Between 2017 and 2019, 14 patients with unacceptable antigens were prospectively matched for acceptable HLA configurations and transplanted. Time on the waiting list of prospectively matched patients (calculated from listing day to transplantation) was compared to waiting time of patients without unacceptable antigens. The lung allocation score for prospectively matched and non-matched patients was calculated. Furthermore, the postoperative course, de-novo DSA and antibody-mediated rejections were analyzed.

**Results:** Prospectively matched patients had a mean waiting time of 37 [7; 155] days compared to 171 [47; 351] days with patients who did not require matching. The mean lung allocation score in matched patients was 48 [40; 75] days and 36 [32; 44] days in non-matched. Seven of 14 patients with unacceptable antigens had a history of a previous lung transplantation. Of the prospectively matched patients transplanted between 2017 and 2019 three developed antibody mediated rejections and five de novo DSA.

**Conclusion:** In our cohort of patients, time on the waiting list was shorter for patients who required a prospective HLA matching. This is the result of half the patients having been listed as highly urgent. Prospective human leukocyte antigen matching of donor organs with recipients is an effective approach to prevent antibody mediated rejections. We are currently in a position of choosing organs immunologically best suited for our recipients rather than having to transplant unmatched organs and routinely desensitizing recipients afterwards.



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**SHERPAK™ – OVERVIEW OF A NEW ORGAN PRESERVATION TECHNOLOGY**

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**Background:** The standard technology for heart preservation for transplantation is cold static storage on ice. No temperature control is performed routinely and therefore lower or higher temperatures can occur leading to injury of the graft. The Paragonix SherpaPak™ Cardiac Transportation System (CTS) (Paragonix Technologies, MA, USA) has been approved in Europe and the USA for clinical use. This single-use disposable device is designed for cold preservation of donor hearts. We report our first clinical experience with the SherpaPak™.

**Methods:** Since November 2018 SherpaPak™ has been used in 6 non consecutive cases in our institution. Decision to use the device was done in procurements with either high-risk donors, long ischemic times or both. Donor risk was calculated with both the Eurotransplant donor heart risk score and the donor heart risk index (both JHLT 2012). Recipient risk was calculated via the IMPACT score (Ann Thor Surg 2011).

**Results:** Median recipient age was 64.5 years. All patients were male and 50% had previous sternotomies (2 VAD patients). Median impact score was 9.5 (17% expected 1 year mortality). All donors were male with a median age of 45.5 years. Median LVEF was 55%. Median norepinephrine support was 0.11 µg/kg/min. Median ET donor risk score was 18 (40% risk of non-acceptance) and median Donor risk score was 7 (18% expected 1-year mortality). Median ischemic time was 290 min. Donor hearts were preserved at a median of 5.5°C temperature. 4 Patients were successfully weaned from bypass at the first attempt with low inotropic support. 2 Patients developed primary graft dysfunction ISHLT Grade 2 and were weaned from bypass via ECMO. Bot heart recovered within 72 h and ECMO could be explanted. All patients could be extubated within 7 days post-transplant and are alive at a median of 5 months post transplant with normal graft function.

**Conclusion:** The Paragonix SherpaPak™ provides consist end temperature during transportation of grafts and could be successfully used with long ischemic times and high risk donor hearts.

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**FIRST TRANSAPICAL TRANSCATHETER AORTIC IMPLANTATION (TA-TAVI) AFTER LONG-TERM HEART TRANSPLANTATION IN AUSTRIA- 5 YEARS OUTCOME**

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**Background:** Valve disease after transplantation is a challenging topic in cardiac surgery, especially in elderly patients after long-term heart transplantation. With improvement of long-term survival degenerative valve diseases like aortic valve stenosis are expected to increase. This case report presents a transapical TAVI in a patient with severe aortic valve stenosis, 23 years after heart transplantation (HTX).

**Methods:** In 1991 a 60 years old patient received a HTX with a 65 years old donor organ. He experienced a normal life with excellent life quality. 23 years later he presented with severe symptomatic aortic stenosis at the age of 83. The patient was considered as too high risk for conventional aortic valve replacement and scheduled for transapical TAVI. The predicted perioperative mortality was 30.76% log EuroScore and 5.36% EuroScoreII.

**Results:** Transapical TAVI with an Edwards Sapien 3 29 mm was successful. Postoperative echo showed an excellent positioning of the valve and no valvular or paravalvular insufficiency. The patient was extubated within the first postoperative day and was transferred to general ward on the second. After an uneventful postoperative stay the patients was discharged home on POD 8. Follow up echocardiography, at 5 years FU, showed a good valve performance, with an AVPMean of 11 mmHg with no paravalvular insufficiency.

**Conclusion:** Transapical TAVI in patients after heart transplantation is an excellent option regarding the age and previous heart surgery. The elderly patients benefit from avoidance of cardio pulmonary bypass and decreased risk for redo-surgery the same site. Increasing life expectancy of patients after heart transplantation and the increase of the donor age, might lead to a higher rate of patients with degenerative valve diseases.

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**INCIDENCE OF MALIGNANCY IN HEART TRANSPLANT RECIPIENTS**

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**Background:** Postoperative survival after heart transplants has improved steadily in recent years and long-term complications are becoming increasingly important. Malignant diseases pose a significant threat to the overall postoperative survival of heart transplant recipients (HTRs). At present, however, data on the incidence and spectrum of post-transplant malignancies in HTRs are scarce and require further evaluation.

**Methods:** 583 HTRs were analyzed retrospectively from 1985 to September 1, 2018 to determine the incidence and entity of post-transplant malignancies by reviewing the heart transplant database of our institution. The collected data of HTRs with and without detected malignancy as well as HTRs with early and late stage cancer were compared and further analyzed.

**Results:** Of 583 HTRs, 67 (11.5%) developed a malignancy after a median of 7.5 (IQR 11) years following transplantation. Amongst these, 57 men (77.5%) and ten women (22.5%) who underwent cardiac transplantation at an average age of 54 (±10.2 SD) years were diagnosed with cancer at an average age of 64.6 (±11.6 SD) years. A total of nineteen cancer entities were diagnosed, with prostate cancer (n = 15), lymphoma (n = 8) and lung cancer (n = 7) occurring most frequently. Besides six (9%) premalignant tumors, 32 (48%) malignancies of an early stage (stage I-II) and fourteen (21%) of a later stage were registered. Fifteen (22.4%) HTRs developed a second post-transplant malignancy. Survival for HTRs with and without a malignancy showed no significant difference (p = 0.62). HTRs with a later-staged malignancy showed a worse overall survival than HTRs with early stage malignancy.

**Conclusions:** A high incidence of post-transplant malignancy was shown in HTRs. The survival of HTRs with early- and later-staged post-transplant malignancies did not differ significantly, whereby in recipients with advanced cancer a decrease can be observed.

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**EVALUATION OF THE MITRA MICROSAMPLING DEVICE FOR TTV MEASUREMENT IN HUMAN WHOLE BLOOD OF ORGAN TRANSPLANT RECIPIENTS**

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**Background:** The apathogenic Torque Teno Virus (TTV) is highly prevalent among solid organ transplant recipients and mirrors the immunocompetence of its host. qPCR based measurement of TTV levels in the peripheral blood is a promising tool on the way towards holistic immunosuppression, but requires out-patient clinic visits for peripheral blood sampling on a regular basis in order to adequately depict TTV kinetics over time. The Mitra® Cartridge micro-sampling device (Neoteryx, California, US) is a novel sampling technique for the remote collection of fixed volume capillary blood and may allow for individualised TTV measurement delays independent of routine visits.

**Methods:** TTV DNA load was assessed in seven patients after solid organ transplantation from EDTA-plasma (200 µL) obtained by peripheral blood sampling and from dried blood (10 µL) collected by capillary blood micro-sampling at the same time using the Mitra® Cartridge device. Dried blood was stored 2 days at room temperature prior to analyses in order to mimic a routine setting of remote blood collection. Samples were analysed in two independent runs of real time-polymerase chain reaction using the same positive and negative controls.

**Results:** Seven patients (4 liver, 3 lung transplant recipients, day 97 (median) after transplantation) had comparable median log levels of TTV DNA in plasma (7.1 log copies/mL) compared to capillary blood (7.1 log copies/mL). Pearson correlation presented that there was a significantly positive correlation between EDTA-Plasma and capillary levels (r = 0.86, p = 0.013).

**Conclusion:** This prove-of-concept study reveals a high correlation of TTV DNA load measured in plasma compared to capillary blood in patients after solid organ transplantation. Volumetric absorptive micro-sampling may be an adequate device to measure TTV levels for remote immunomonitoring in an outpatient transplant recipient cohort, but larger sample sizes will be needed to confirm our preliminary data.

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**TRANSITION WORKSHOP FOR YOUNG ADULTS WITH CHRONIC NEPHROLOGICAL DISEASES***S.-H. Hemberger, K. Roithner**Department of Pediatric Nephrology, University Clinic for Pediatric and Adolescent Medicine, AKH, Vienna, Austria*

**Background:** It is estimated that around 190000 children and adolescents in Austria suffer from a severe chronic disease, including various types of kidney disease. Sooner or later, chronic renal insufficiency necessitates renal replacement therapy and subsequent kidney transplantation. Since medical care has steadily improved over the past few decades, many patients who previously did not reach adulthood or who had many limitations due to the severity of their illness have been able nowadays to integrate their illness into their daily lives. Therefore, a structured, individually adapted and accompanied change of care (= transition) with a multiprofessional team is internationally recognized as "best practice".

**Methods:** The department of Pediatric Nephrology (University Clinic for Pediatric and Adolescent Medicine, AKH Vienna) in cooperation with the

Kaiser-Franz-Josef-hospital has examined the effect of a workshop on transition for transplanted, dialysis-dependent and chronic renal failure patients aged 18–25 years. At the beginning, after 6 and 12 months, respectively, the participants were asked about disease and medication knowledge, disease activity, quality of life, disease processing, resources, self-management and self-efficacy by means of questionnaires. In the course of a one-day workshop, the patients were trained by a multiprofessional team to get informed how to deal with their illness.

**Expected Results:** The collected data of disease activity, disease and medication knowledge, self-dependence and positive disease handling have a positive impact on quality of life. Similarly, an intensive examination of the topic of transition should have a positive influence on the disease.

**Conclusions:** Adolescent patients often have little interest in acquiring disease and medication knowledge and are usually not ready for a change of care at the age of 18. In addition to health consequences for the individual, economical consequences are also relevant if patients have to deal with the process of transition without professional help.