ORAL PRESENTATIONS

PL01 | COVID-19 and Transplantation

PL01-02

ORGAN DONATION AND TRANSPLANTATION IN TIMES OF THE SARS-COV-2 (COVID-19) PANDEMIC: THE EUROTRANSPLANT PERSPECTIVE

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Introduction: The SARS-CoV-2 pandemic has spread worldwide at an unprecedented speed, triggering drastic changes in routine patient care. This article describes the impact of the first pandemic wave on post-mortem organ donation and transplantation activities in the Eurotransplant (ET) region.
Methods: The study period covers March and April 2020 and the corresponding reference period in 2019. The epidemiological COVID-19 data were retrieved from the John Hopkins University data resource center. Donor and transplant data were extracted from the ET database.
Results: With the increase in COVID-19 cases, postmortem organ donation (-91) and total transplant activity (-272) decreased significantly in whole of ET, with significant regional differences. On top of the lower transplantation activity due to the lower organ donation rate, there was a deliberate decision by transplant physicians not to perform non-urgent transplants.
Conclusion: Pandemic-related cuts in treatment capacity led to a dramatic decline in organ donation and transplantation. A corresponding increase in waiting list mortality is expected.

S10 | PREPARATION AND AFTERCARE LIVER TRANSPLANTATION

S10-05

ELEVATED DONOR-DERIVED CELL-FREE DNA DURING SUBCLINICAL T-CELL MEDIATED REJECTION AFTER LIVER TRANSPLANTATION

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Introduction: Subclinical T-cell mediated rejection (subTCMR) is commonly found even late after liver transplantation (~25%), associated with upregulation of rejection associated transcripts and can only be diagnosed through liver biopsies (1, 2). Despite having a good prognosis even if left untreated, subTCMR should be excluded before immunosuppression minimization attempts are undertaken during individualized immunosuppression. The analysis of graft cell-free DNA (GcfDNA) could provide a non-invasive tool to identify subclinical graft injury.
Methods: Samples with subclinical graft injury (liver enzymes $\leq$ 2 upper limit of normal) were taken from the prospective protocol biopsy program after liver transplantation at our centre. Liver biopsies were extensively reviewed for histological signs of graft injury including subTCMR (RAI$\geq$1+1+1) and histological criteria for immunosuppression minimization (HCmini) according to Demetris et al. (3). Clinically relevant TCMR (clinTCMR; liver enzymes > 2x ULN) was used as a comparator group. We used digital droplet PCR to measure GcfDNA in recipient plasma samples paired to liver biopsies (4). The Mann-Whitney-U test was used for statistical analysis.
Results: The mean GcfDNA was 3.4% in patients with no histological signs of rejection (NHR group (N=22)), 6.2% in the subTCMR group (N=15) and 25.6% in the clinTCMR group (N=19). There was a significant difference between the mean GcfDNA of each group (NHR vs. subTCMR p=0.021, NHR vs. clinTCMR p<0.001, subTCMR vs. clinTCMR p<0.001). Considering possible individualization of immunosuppression, we analysed 21 samples where HCmini were satisfied and 33 samples where they were not. The mean percentage of GcfDNA was 3.2% for the former and 5.1% for the latter (p=0.034).
Conclusion: GcfDNA seems to be a promising marker for the non-invasive monitoring of subclinical liver graft injury in this small pilot study and thereby a potential clinical tool to facilitate individualized immunosuppression after liver transplantation. More extensive testing is currently ongoing.

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S13 | MINIMALLY INVASIVE TECHNIQUES IN TRANSPLANTATION SURGERY

S13-01

PSYCHOSOCIAL PRE-TRANSPLANT SCREENING WITH THE TRANSPLANT EVALUATION RATING SCALE CONTRIBUTES TO PREDICTION OF SURVIVAL AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Hematopoietic stem cell transplantations (HSCT) is a challenging treatment. Integrating assessment of psychosocial aspects is important because immunosuppressant adherence is essential for prevention of graft-versus-host disease (GvHD). The aim of this study is to explore the predictive value of the pretransplant psychosocial screening instrument Transplant Evaluation Rating Scale (TERS) for mortality in a three-year follow-up.
Methods: A prospective study was performed between 2012 and 2017 including 61 patients classified by psychosocial risk factors as low (TERS = 26.5–29) and increased-risk group (TERS = 29.5–79.5). Both groups were compared regarding mortality until 36 months after transplantation and secondary outcomes (self-reported barriers of immunosuppressant intake: Medication Experience Scale for Immunosuppressants (MESI); incidence/grade of GvHD).
Results: The increased-risk group (n=28) showed significantly worse cumulative survival in the outpatient setting (from three months to three years after HSCT) (Log Rank (Mantel Cox) p=0.029) compared to low-risk group (n=29) but there was no significant result for the interval immediately after HSCT until 3 years afterwards. There were no significant correlations between TERS and grade of GvHD or MESI.
Conclusion: Pre-transplant screening with TERS contributes to prediction of survival after HSCT. The reason remains unclear, since TERS did not correlate with GvHD or MESI. The negative result regarding the interval immediately after HSCT until 3 years could be caused by the intensive in-patient setting with mortality which is explained rather by biological reasons than by nonadherence. Assessment with TERS adds to the detection of high risk patients for interventions to improve survival.

S16 | THE CHALLENGES OF PAEDIATRIC TRANSPLANTATION

S16-04 SAFETY AND TOLERABILITY OF DONOR-DERIVED MESENCHYMAL STEM CELLS IN PAEDIATRIC LIVING-DONOR LIVER TRANSPLANTATION: THE MYSTEP1 STUDY

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Introduction: Calcineurin inhibitor (CNI) toxicity leads to significant morbidity and impairs quality of life of liver transplant (LT) recipients. Mesenchymal stromal cells (MSCs) have potent immunomodulatory properties, which may promote graft tolerance and ameliorate toxicity of exposure to high-dose CNI. The MYSTEP1 trial aims to investigate the safety and tolerability of donor-derived MSCs in LT.
Methods: We conducted a non-randomized, open-label, prospective, single-centre study [1]. MSCs from living donors were administered by intraportal and intravenous (day 2) infusion. Assessing patient's safety, we screened for treatment-emergent adverse events by applying the paediatric infusional toxicity score (adapting [2]) focussing on the injury of lungs, liver allograft and systemic reactions. Secondary, we assessed the efficacy of MSC treatment, measured by the individual need for immunosuppressive medication (IS) and the incidence of biopsy-proven acute rejection (BPAR).
Results: Seven Children (median age = 6 months), diagnosed with biliary atresia (n=5), BSEP deficiency (n=1) and PSC (n=1), were included in this trial. The participants received 2 doses of $1x10^6$ MSCs/kg body weight from the living LT donor. The 1st infusion was administered in the donor portal vein during LT. Transit time flow measurement of the portal flow, before and after portal cell infusion, did not detect any flow impairment (134 vs 171 ml/min/100g; p=0,47). We did not observe an acute severe treatment-emergent event including acute thromboembolism. However, late thrombosis of extrahepatic portal vein occurred in one patient. Further, one participant developed EBV-positive PTLD 5 months post LT while on standard CNI dosage. All participants received initially standard IS following our centre's LT protocol, including tacrolimus and steroids. Protocol biopsies 6 months post LT were unremarkable in all cases so that we were able to reduce IS. We did not observe any case of BPAR.
Conclusion: Our preliminary data show that the intraportal and intravenous MSC infusion was safe. There were no acute infusion-related adverse events. We were able to reduce CNI trough levels without detecting BPAR, but efficacy has to be further evaluated.
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S16-05 CARDIAC ALLOGRAFT VASCULOPATHY IN ANGIOGRAPHY AND OCT: AGE- AND SEX-DEPENDENT RISK FACTORS IN ADULT AND PEDIATRIC PATIENTS

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Introduction: Assessment of risk factors predicting cardiac allograft vasculopathy (CAV) is most relevant to improve CAV prevention after heart transplantation (HTx). Few risk factors have been validated in pediatric HTx patients and current recommendations regarding medical CAV prevention are largely based on data obtained in adults [1]. Yet, whether the predictive value of current risk factors depends on age or sex of HTx patients is unknown. Here, we used optical coherence tomography (OCT), a safe intracoronary imaging tool with highest spatial resolution for early CAV detection, and tested the age- and sex-dependency of established risk factors in a cohort of HTx patients.
Methods: We performed a retrospective analysis of CAV in pediatric and adult HTx patients who underwent both angiography and OCT as part of post-transplant follow-up between 12/2013 and 10/2019 at the Ludwig-Maximilians University of Munich. CAV was defined as angiographically manifest CAV and/or intimal hyperplasia (IH) in OCT. IH was defined as intimal thickness>0.3mm. Findings were correlated with the prevalence of risk factors.
Results: 102 patients were included. 36 patients (35.3%) were aged < 18years and 66 patients (66%) ≥18years at the time of OCT. 70 patients (68.6%) were male. Odds Ratio (OR) of dyslipidemia was 6.41 with 95% CI [2.36–17.46]. OR of dyslipidemia was higher in adults (17.00 [2.09–138.08]) than in pediatric patients (5.32 [1.17–24.14]), and in female (9.00 [1.72–46.99]) compared to male patients (6.42 [1.68–24.53]). Obesity increased the risk for CAV prevalence in all patients (3.17 [1.07–9.39]), whereas diabetes mellitus and arterial hypertension did not. Male sex (2.46 [1.05–5.80]), age at OCT (1.05 [1.02–1.07]), age at HTx (1.04 [1.02–1.06]) and post-transplant time (1.10 [1.01–1.18]) increased the risk for CAV prevalence in all patients.
Conclusion: In our study, we could show that the most important risk factor for CAV prevalence in pediatric and adult HTx patients was dyslipidemia. Whereas non-modifiable factors such as age, post-transplant time and donor parameters represent a comparable risk in all patients, dyslipidemia particularly increases the risk for CAV in female and adult patients.
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S16-06 ASSOCIATION OF GRAFT SURVIVAL WITH TACROLIMUS EXPOSURE AND LATE INTRA-PATIENT TACROLIMUS VARIABILITY IN PEDIATRIC AND YOUNG ADULT RENAL TRANSPLANT RECIPIENTS

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Introduction: Adolescent and young adult age is a high-risk window with an alarmingly increased likelihood of premature kidney graft loss due to rejection. We hypothesized that a more intense and less variable exposure to the main immunosuppressant tacrolimus could counteract the enhanced immune reactivity in the high-risk age group of adolescents and young adults and result in better graft survival.
Methods: Using the large database of the Collaborative Transplant Study we analyzed whether a more intense and less variable exposure to tacrolimus could counteract this young-age-related enhanced immunoreactivity. Mantel Cox log-rank (with trend) test was used for analysis of the impact of both tacrolimus trough levels as well as intra-patient variability (IPV) of tacrolimus trough levels on graft survival.
Results: Graft survival at year 5 post-transplant differed significantly among the age groups; patients between 0–5 or 6–11 years of age had a significantly better graft survival during post-transplant years 2–5 than patients between 12–17 or 18–23 years ($p<0.001$), while graft survival in patients aged 24–29 and 30–34 years was intermediate. Kidney graft recipients aged 12–23 years (n=964) with a 1-year tacrolimus trough level between 4.0–10.9 ng/mL had a 5-year graft survival rate of 85.1%, significantly better than the poor 66.1% rate in patients with a trough level below 4.0 ng/mL who showed a 2.38-fold increased risk of graft loss in the multivariable analysis ($p<0.001$). This association was not apparent in young children aged 0–11 years (n=455) and less pronounced in adults aged 24–34 years (n=1,466). However, an IPV of tacrolimus trough level ≥1.5 at post-transplant years 1 and 2 was associated with an increased graft loss risk in both 12–23- as well as 0–11-year-old recipients ($p<0.001$ and $p=0.045$). Patients with high IPV made up as many as 30% of kidney graft recipients.
Conclusion: Our data indicate that a more intense and less variable exposure to the main immunosuppressant tacrolimus later than 1 year post-transplant is associated with a better 5-year graft survival especially in adolescents and young adults, presumably by counteracting the enhanced alloreactivity in this high-risk age group.
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S17 | PERSISTENT VIRUSES UNDER IMMUNOSUPPRESSION

S17-05 MONITORING OF EBV-SPECIFIC IMMUNITY AND HUMORAL MILIEU FACTORS AS EARLY MARKERS FOR PTLD DEVELOPMENT IN EBV POSITIVE HIGH RISK PEDIATRIC SOT PATIENTS – FIRST RESULTS OF THE EB-VISI (EPSTEIN-BARR VIRUS-SPECIFIC IMMUNITY) STUDY

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) represent a large problem in pediatric solid organ transplant (SOT) recipients.[1] In particular, following heart and lung transplantation in children there is a 15–20% risk of PTLD development within the first 5 years.[2,3] There is no standard monitoring for PTLD. EBV infection in EBV-negative patients is a major risk factor for PTLD development;[4] however, monitoring of EBV load in peripheral blood alone is not sufficient to identify patients at high risk.[5]
We aim at establishing a set of cellular and / or serologic markers with potential value in predicting development of EBV+ PTLD in high risk SOT patients.
Methods: We set up a prospective pilot study to identify different markers that would be informative to examine in further transplanted patients. The follow-up study was extended to establish a cohort of 100 pediatric heart and lung transplant patients. Blood samples were taken in 2–4 month intervals from asymptomatic EBV+ participants. Samples were analyzed for 1) phenotype of immune cells by flow cytometry, 2) frequency of EBV-specific T cells by interferon-gamma ELISPOT assay using various EBV antigens, and 3) for humoral factors. Data were analyzed for mean, standard deviation and 95% confidence interval.
Results: So far 87 EBV+ patients have been included and 9 patients with EBV+ PTLD. Sex ratio is balanced. Median follow up after transplantation is 5.3 years. All patients received their SOT during childhood; 20 patients are now >20 years old, while the remaining are children and adolescents. PTLD patients were at median 5 years old and 1.1 years after SOT. We started to analyze the intra- and interindividual consistency of absolute immune cell counts and generated reference values for this patient cohort. The cellular immune response to several EBV antigens analyzed by interferon-gamma ELISPOT was highly variable.
Conclusion: This ongoing study aims at elucidating factors for early diagnosis of high PTLD risk in EBV+ SOT recipients. Early results demonstrate the feasibility of complex cellular analysis and first insights into the immune system under immunosuppression.

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S17-06 IL-10 PROMOTES CHRONIC BK-VIRUS INFECTION AND HLA CLASS I ANTIBODY FORMATION IN RENAL TRANSPLANT RECIPIENTS

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Introduction: In a randomized prospective renal transplant study, we found that IL-10 plays a key role in chronic BKV infection. Tacr/ERL treatment significantly downregulated IL-10 responses and resulted in the lowest BK viremia incidence compared to CsA/MMF and Tacr/MMF treatment. As IL-10 acts as a potent B cell growth and differentiation factor, we wondered whether increased IL-10 responses in chronic BK-virus infection might promote HLA antibody formation.
Methods: We analyzed intracellular cytokine responses, CD4+ T helper function and in-vitro B cell responses pretransplant and up to 24 months posttransplant. 105 renal transplant recipients were randomized to a CsA/MMF (n=35), Tacr/MMF (n=37) and Tacr/ERL (n=33) regimen, respectively. Luminex-based HLA class I and II and MICA antibody screening was performed pretransplant and 1 and 2 years posttransplant.
Results: In patients developing BK viremia, posttransplant HLA and MICA antibody formation was not increased compared to patients without BK viremia ($p \geq 0.256$). However, pretransplant increased CD4, CD8 and CD14 cell IL-10 production was significantly related to HLA class I antibody formation in CsA/MMF or Tacr/MMF treated patients (CD4 and CD8 cells: 1 year and 2 years, $p<0.0005$; CD14 cells: 1 year, $p=0.013$) but not in Tacr/ERL treated patients. Compared to CsA/MMF and Tacr/MMF patients, Tacr/ERL patients showed downregulated IL-10 responses (CD4 cells: $p=0.009$, 1 year; CD19 cells: $p=0.002$, 4 months; CD14 cells: $p=0.048$, 2 years) and increased T-dependent B cell responses ($p=0.004$, 4 months; $p=0.019$, 1 year) posttransplant.
Conclusion: Patients developing BK viremia did not show a generally increased risk of HLA and MICA antibody formation within 2 years posttransplant. However, increased in-vitro IL-10 production pretransplant was significantly associated with posttransplant HLA class I antibody formation, with the exception of Tacr/ERL patients who showed downregulated IL-10 responses posttransplant.

S18 | ANTIBODY DIAGNOSTICS IN KIDNEY TRANSPLANTATION 1

S18-07 DEVELOPMENT OF DE NOVO ANTI-HLA-DSA IN RENAL TRANSPLANT PATIENTS DEPENDS ON CYP3A5 GENOTYPE

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Introduction: The single nucleotide polymorphism of CYP3A5 6986A>G is related to reduced metabolizing activity of tacrolimus. CYP3A5 expressers have higher tacrolimus clearance and lower through concentrations than homozygous nonexpressers. However, reports on the influence of CYP3A5 genotype on allograft survival and acute rejection after kidney transplantation are controversial. We investigated the link between CYP3A5 polymorphism and renal allograft outcome and incidence of viral and bacterial infections.
Methods: A retrospective single center study was performed on 412 kidney transplant patients who were transplanted 2011–2015 and received tacrolimus. We determine the CYP3A5 genotype by PCR and assessed its effect on graft survival, rejection rate and occurrence of de novo DSA as well as risk of infections during the first 5 years after transplantation.
Results: We identified 70 (17%) of 412 patients having the expresser genotype. CYP3A5 genotype had no impact on clinical outcome such as allograft failure and T-cell mediated as well as antibody-mediated rejection. Indeed, the percentage of patients with de novo anti-HLA antibodies and DSA was significantly increased in the CYP3A5 expresser group. De novo anti-HLA antibody- und DSA-free survival rates were lower in expressers compared with nonexpressers. Additionally, in univariate and multivariate analysis CYP3A5 expresser status was found to be an independent risk factor for de novo DSA development. No differences in infection rates posttransplant between both groups were observed.

Conclusion: CYP3A5 expresser genotype is an independent risk factor for de novo DSA development. Early identification of recipients carrying CYP3A5 expresser genotype following genotype–based dose adjustment of tacrolimus immediately after renal transplantation might be a useful strategy to reduce the risk of de novo DSA production and improve long-term allograft survival.

S19 | IMMUNOSUPPRESSION KIDNEY

S19-03 PATIENT CHARACTERISTICS OF LIVING KIDNEY DONORS OVER THE PAST FIVE DECADES

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Introduction: Living kidney donation is the therapy on choice for many end-stage renal disease patients. In view of a changing landscape in renal transplantation with increasing organ shortage selection criteria for potential donors alter. The objective of this study is to evaluate the shift of living kidney donor characteristics and outcome during the last decades.
Methods: A cohort study including 765 living kidney donors donating from 1967 to 2016 was established. Primary objective was to identify variation of donor age. Secondary objectives were to evaluate changing acceptance criteria concerning accompanying diseases.
Results: Living kidney donor age increased from 34.9±11.5 to 53.2±10.2 years. The percentage of donors aged > 65 years augmented from 0% to 11.4%. Numbers of recipients with co-morbidities at the time of donation increased. Percentage of obese donors and hypertensive donors rose up to 18.6% and 37.0%, respectively. Smoking was obvious in 37% of the donors. Outcome data revealed a stable renal function. De novo hypertension is a common problem in more than half of the donors in the long-term follow-up. Malignancy and cardiovascular events were the main reason for death with a functioning graft.
Conclusion: A detailed analysis of donor characteristics of living kidney donors over the last 5 decades revealed increasing age, body mass index, number of co-morbidities in the donor cohort. Health care professionals, recipients and potential donors should be encouraged to understand the possible risks to make an informed choice on donation.

S19-04 MICROVASCULAR INFLAMMATION IS A RISK FACTOR IN KIDNEY TRANSPLANT RECIPIENTS WITH VERY LATE CONVERSION FROM CALCINEURIN INHIBITOR-BASED REGIMENS TO BELATACEPT

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Introduction: Immunosuppressive strategies in long-term renal allograft recipients with progressive graft dysfunction are controversial. Although belatacept (Bela) has been associated with increased acute rejection rates early post-transplant, it may avoid CNI toxicity, non-adherence and risk of donor-specific antibody (DSA) formation. Only few data are available on switching immunosuppression in patients at increased immunological risk and at later stages after transplantation.
Methods: 30 long-term kidney transplant recipients (KTR), including 2 combined pancreas-KTR converted from CNI to belatacept >60 months after transplantation with moderate to severe graft dysfunction (GFR≦45 mL/min) were analyzed, retrospectively. Main reasons to switch were CNI-toxicity and non-adherence. Positivity for DSA at conversion was 46.7%. Biopsies were classified according to the Banff 2015 criteria. Group differences were assessed in a univariate analysis using Mann Whitney U or Chi square test, respectively. Multivariate analysis of risk factors for treatment failure was performed using a binary logistic regression model including significant predictors from the univariate analysis. 56 control KTR matched for donor and recipient characteristics were used as a control cohort.
Results: Bela cohort patient survival at 12/24 months was 96.7%/90%, while graft survival censored for death was 79.3%/66.7%. In patients with functioning grafts, median GFR improved from 22.5 mL/min to 24.5 mL/min at 24 months (mean ΔGFR of +1.8 ± 7.9 mL/min). From univariate analysis of multiple risk factors for graft loss, GFR<25mL/min (p=0.042) and Banff microvascular inflammation (MVI) sum score ≧2 (p=0.023) at conversion were significant at 24 months. In contrast, control cohort patient and graft survival showed comparable results at 24 months, but, albeit with a lower percentage of DSA positivity (33.9%), no increase of mean GFR in patients with functioning grafts (ΔGFR of −3.6 ± 8.5 mL).
Conclusion: Rescue therapy with conversion to belatacept is feasible in patients with worsening renal function, even many years after transplantation. The benefit in patients with MVI and severe GFR impairment remains to be investigated.

S20 | COVID-19

S20-02 TRANSPLANT PATIENTS ARE ABLE TO MOUNT SARS-COV-2-REACTIVE T-CELL RESPONSE WITH THE MAGNITUDE AND FUNCTIONALITY COMPARABLE TO NON-IMMUNOSUPPRESSED PATIENTS

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Introduction: The optimal management of COVID-19 in transplant patients is not defined so far. The major concern is the ability of transplant patients to generate a sufficient antiviral response under immunosuppressive treatment.
Methods: Here, we analysed T-cell immunity directed against Spike, Membrane and Nucleocapsid proteins of SARS-CoV-2 in a small cohort of 6 transplant patients (TP) with COVID-19 in comparison to 28 non-immunosuppressed patients (NIP).
Results: The median patient age of transplant cohort (3 renal transplant, 1 lung, and 1 combined liver-kidney and 1 pancreas-kidney) as well as gender did not differ from NIP. We also did not find statistical differences for the time between the diagnosis of COVID-19 and analysis of T-cell immunity between the two cohorts. Notably, despite immunosuppressive therapy, we were able to detect a strong antiviral response in transplant patients. TP generated SARS-CoV-2 reactive T-cells against all three proteins with predominance of CD4 + T cells with pro-inflammatory Th1 phenotype. Moreover, SARS-CoV-2 reactive CD4 + and CD8 + T cells were able to produce multiple pro-inflammatory cytokines demonstrating their potential protective capacity. Of interest, the frequencies and cytokine production patterns of SARS-CoV-2 reactive T-cells did not show any differences between TP and NIP.
Conclusion: A strong polyfunctional T-cell response directed against all three SARS-CoV-2 proteins can be generated in transplant despite immunosuppressive treatment. In comparison to non-immunosuppressed patients, the antiviral immunity is non-inferior. Since the dosage of immunosuppression in analysed patients was reduced, further studies are required to assess the antiviral immunity under standard immunosuppression.

S20-03 PRE-EXISTING SARS-COV-2 REACTIVE T CELLS IN RENAL TRANSPLANT PATIENTS

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused unprecedented public health and economical challenges worldwide.

Cellular immunity is known to be crucial for the virus clearance. Recent data demonstrate pre-existing SARS-CoV-2-reactive T cells in samples of healthy blood donors collected before SARS-CoV-2 pandemics. The presence of these potentially protective T cells in SARS-CoV-2 naive population can be explained by cross-reactivity to the endemic common cold coronavirus. Whether such cells are also detectable in immunosuppressed patients is not known so far.
Methods: We analysed the presence of SARS-CoV-2-cross-reactive T cell immunity in samples of 10 renal transplant patients (RTX) collected in 2019 before the onset of SARS-CoV-2 pandemics. Samples of 10 non-immunosuppressed/immune competent SARS-CoV-2 naive patients matched to transplant patients were analysed as controls. T-cell reactivity against Spike-, Nucleocapsid-, and Membrane- SARS-CoV-2 proteins were analysed by multiparameter flow cytometry.
Results: 50% of analysed RTX showed CD4 + T-cells reactive against at least one SARS-CoV-2 protein. CD8 + T cells reactive against at least one SARS-CoV2 protein were demonstrated in 30% of RTX. Notably, the detected cells were of differentiated memory phenotype producing several Th1 cytokines including IFNg, TNFa, IL-2, as well as Granzyme B. The frequencies and cytokine expression pattern of SARS-CoV-2 reactive T-cells did not differ between transplant and non-transplant cohorts.
Conclusion: Despite immunosuppressive treatment and underlined renal disease, transplant patients were able to generate cellular immunity cross-reactive to SARS-CoV-2. The magnitude and functionality of the pre-existing immunity was non-inferior compared to the immune competent cohort. Although several pro-inflammatory cytokines were produced by the detected T cells, further studies are required to prove their antiviral protection.

S20-04 OUTCOMES OF COVID-2019 IN RENAL TRANSPLANT RECIPIENTS VERSUS CHRONIC HEMODIALYSIS PATIENTS: ANALYSIS OF A REGIONAL COHORT

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Introduction: SARS-CoV-2 causing COVID-19 has rapidly spread around the world with the first German cluster emerging in the area around Heinsberg. Mortality rates are reported to vary between 1–14%. While end-stage renal disease is a putative risk factor for adverse outcomes of COVID-19, the impact of carrying a renal transplant (KTX) versus being on chronic hemodialysis (HD) is not well defined.
Methods: We describe a cohort of 21 patients on renal replacement therapy (7 KTX and 11 HD treated for COVID-19 plus 3 asymptomatic HD carriers of SARS-CoV-2) in the Heinsberg area. Data were collected systematically via the two local dialysis care providers specifically serving the area as well as the local tertiary care hospital and renal transplant center at the University Hospital Aachen. All patients were followed for the entire course of the disease over a median of 66 days (40–71 IQR). Medication, comorbidities and clinical outcome were recorded.
Results: Of the seven KTX patients four were hospitalized with an acute respiratory distress syndrome (ARDS), three of which died; two of fulminant multiorgan failure and one of multiple complications of intensive care medicine after prolonged weaning and viral encephalitis. These three patients also developed acute kidney injury requiring renal replacement therapy. In all hospitalized KTX recipients MPA was stopped directly upon admission while CNIs were held only as a more severe clinical course ensued. Of the 11 HD patients with COVID-19 six were hospitalized. Three developed ARDS, two of them died. While requirement for hospitalization and duration of viral RNA-shedding were similar in KTX versus HD patients, the duration of illness and of hospitalization were longer in the KTX group by 8 and 14 days, respectively.
Conclusion: COVID-19 has a variable course in renal transplant recipients as well as patients on chronic hemodialysis ranging from (almost) asymptomatic infection to severe ARDS with lethal outcome. Patients on renal replacement therapy seem to have a more favorable outcome than patients after kidney transplantation (mortality 18% vs. 43% following KTX). Early reduction of immunosuppression did not seem to prevent mortality.

S20-05 SARS-COV-2 INFECTION RATES MAY BE INCREASED IN DIALYSIS PATIENTS ON THE TRANSPLANT WAITING LIST

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Introduction: Chronic dialysis represents a state of immunocompromise. Unlike the general population, patients cannot observe strict isolation as they have to visit the dialysis unit three times per week and therefore potentially increase their risk of contracting an infection with SARS-CoV-2. This represents a special dilemma for patients awaiting renal transplantation. Active infection is considered a contraindication whereas renal transplantation may be considered for dialysis patients who have recovered.
Methods: Referring dialysis physicians were surveyed to report non-transplantable and SARS-CoV-2 infected patients. The incidence of PCR-confirmed SARS-CoV-2 cases among dialysis patients on the kidney transplant waiting list was compared with a non-matched population in the referral area (Bavaria).
Results: As of May 1st 2020, 42,489 individuals of the general population (0.33%) in Bavaria had been infected with SARS-CoV-2. At the same time, 4 out of 331 patients (1.3 %) on our waiting list contracted an infection with SARS-CoV-2. 2 were asymptomatic, one required inpatient treatment. None died due to COVID-19. 313 patients were without clinical signs of SARS-CoV-2 infection. Thereof 60 were also negative on PCR-testing due to infection in the respective centre. 5 patients had died during the pandemic due to non-COVID-19 related causes. For 18 patients no information on SARS-CoV-2 was available.
Demographic data are given in table:

	Age (years)	male	Dialysis vintage (days)
Patients without SARS-CoV-2	53	208/119	1910
Patients with SARS-CoV-2	48	4/4	2181

Thus, patients on the renal transplant waiting list had a 3.9-fold higher incidence of SARS-CoV-2 infection (p=0.02).
Conclusion: Although epidemiological statements based on this survey are deemed uncertain, the incidence of symptomatic SARS-CoV-2 infections in dialysis patients on the waiting list seems to be slightly higher. The absolute numbers are low, however, and the observed courses of disease are mild.

S21 | ANTIBODY DIAGNOSTICS IN KIDNEY TRANSPLANTATION 2

S21-05 INCREASE IN CYTOTOXIC HLA ANTIBODIES IN PRETRANSPLANTED PATIENTS DURING THE FIRST YEAR ON THE WAITING LIST

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Introduction: Crossmatches prior to deceased donor transplantation are usually performed using the serum from the last quarterly antibody testing. Increased cytotoxic antibodies since the last screening could cause an unrecognized risk of rejection.
Methods: All CDC screening results between 2000 and 2019 were evaluated. Increments in panel reactivity of at least 10%-points were considered as PRA-increase. Possible trigger events were compiled from clinical records and questionnaires sent to the patients' nephrologists.
Results: Evaluating 16.740 tests, 84 PRA-increases due to new or boostered antibodies were detected. Common immunizing events like transfusions, pregnancies or removal of a previous transplant accounted for 31 cases (37%), while none of these factors was reported for 13 patients and only insufficient information could be obtained for 40 patients. Rising PRA-values were more frequent in patients with previous transplants (1.3% of tests compared to 0.2% in first-time patients). This difference was especially pronounced during the first year on the waiting list, when 2.0% of pretransplanted patients formed additional HLA-antibodies. These antibodies were mostly caused by decreased immunosuppression and/or transplant nephrectomy (12 out of 26 cases, 46%), while transfusion and pregnancies without other risk factors accounted for only 2 cases (8%). No classical immunizing event was reported for three patients, and in nine cases only insufficient information was available.
Conclusion: Increases of CDC-reactive antibodies occur most frequently in pretransplanted patients during their first year on the waiting list. These increases are often not preceded by classical immunizing events like transfusions or pregnancies, but by reduction of immunosuppression. In several cases, no triggering event could be determined. Patients presenting for kidney transplantation should be interrogated about possible reduction of immunosuppression within the preceding months. Especially within the first year on the waiting list, performing a crossmatch with a fresh serum might be indicated to prevent an increased immunological risk due to cytotoxic antibodies not present in the last quarterly serum.

S23 | TISSUE ENGINEERING

S23-04 ESTABLISHMENT OF IN-VIVO PARTIAL LIVER DECELLULARIZATION IN RATS: THE PREREQUISITE FOR IN-VIVO LIVER ENGINEERING

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Introduction: In-vivo liver decellularization has become an interesting strategy to study in-vivo repopulation of a liver scaffold (Pan, IntJBiochem& Cellbio 2016). However, up to date, long term survival after in-vivo liver lobe decellularization has not been reported yet. Our aim here is to establish an in-vivo partial liver lobe decellularization model with long term survival.
Methods: 12 rats were enrolled. An in-vivo circuit bypass was created only through the left lateral liver lobe in living rat (Wang. All cells were chemically removed by perfusing the lobe with detergents. The quality of the decellularized scaffolds (n=4) were analysed by H&E staining, immunohistochemical staining and micro CT scanning. After in-vivo blood reperfusion of the decellularized scaffolds, the rats (n=8) were allowed to recover from anaesthesia for survival analysis.
Results: In H&E staining, no cellular but only structural components were observed in the decellularized scaffolds, indicating that the lobe was completely decellularized. Immunohistochemical staining for elastin demonstrated that elastic components remained in the scaffold. The three-dimensional vasculature was preserved as confirmed by micro-CT scanning. Large amounts of blood cells in the blood reperfused liver scaffold were observed by histological staining, indicating the decellularized scaffold was perfused with blood. All rats survived for more than one week (n=8/8).
Conclusion: We achieved successful establishment of an in-vivo isolated liver lobe decellularization model with long term survival in living rats. This technique is needed as a solid foundation for further study of in-vivo organ engineering
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S24 | MONITORING OF IMMUNOSUPPRESSION

S24-03 MONITORING OF GENE EXPRESSION IN TACROLIMUS-TREATED DE NOVO RENAL ALLOGRAFT RECIPIENTS FACILITATES INDIVIDUALIZED IMMUNOSUPPRESSION – RESULTS OF THE IMAGEN STUDY

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Introduction: The expression of nuclear factor of activated T-cells (NFAT)-regulated genes in the peripheral blood has been suggested as a potentially useful immune monitoring tool to individualize tacrolimus (Tac) therapy. The aim of the present study was to characterize the possibility and clinical utility of monitoring of residual NFAT-regulated gene expression in renal allograft recipients in a multicenter approach.
Methods: The IMAGEN study enrolled 64 de novo renal transplant recipients from three European centers. All patients were treated with Tac, mycophenolic acid, and corticosteroids. NFAT-regulated gene expression (NFAT-RGE; IL-2, IFN-g, GM-CSF) was evaluated by quantitative real-time PCR in whole blood samples at day 7, month 1, 2, 3, and 6 after transplantation.
Results: Altogether, 60 patients could be evaluated. Tac concentrations (C0 and C1.5) correlated inversely with gene expression ($p<0.001$). NFAT-RGE showed a high interindividual variability (1 to 61%). RGE increased in the first two months from 16±9% to 34±21%. Patients (n=20) with high residual gene expression (NFAT-RGE≥30%) were at the increased risk of acute rejection in the following months (35% vs 5%, p=0.002), whereas patients (n=40) with low residual gene expression (NFAT-RGE<30%) showed a higher incidence of viral complications, especially cytomegalovirus and BK virus replication (52.5% vs 10%, p=0.001).
Conclusion: NFAT-RGE was confirmed as a potential non-invasive early predictive pharmacodynamic marker in the immediate post-transplant period for the risk of acute rejection and infectious complications in Tac-treated renal allograft recipients. Monitoring of NFAT-RGE may provide additional useful information for physicians to achieve individualized treatment adjustments based on the immunomodulatory effect of Tac, thus preventing serious clinical events. The method of NFAT-RGE measurements can be applied in trials with multicenter approach.

S24-04 TACROLIMUS TOXICITY AND LOSS OF RENAL FUNCTION FOLLOWING HEART TRANSPLANT DEPENDS ON C/D RATIO

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Introduction: Immunosuppressive therapy with tacrolimus (tac) is a common standard after solid organ transplantation. Significant side effects are especially nephro- and neurotoxicity. To identify patients who are at increased risk of developing nephropathy, Thölking et al. have already established in patients after kidney and liver transplantation, the concentration / dose ratio (C/D ratio) as a meaningful clinical tool. Renal failure after heart transplantation is a major factor in mortality and morbidity. In the present study, the C/D ratio in patients after heart transplantation was evaluated for the first time.
Methods: A retrospective monocentric observational study was carried out. The study included 159 patients in the 2007–2018 period who had not received a prior transplant, who had not undergone a combined organ transplant, and who had been taking tac for at least 6 months. The initial immunosuppression therapy consisted of tac (Prograf), mycophenolate mofetil and prednisolone. The statistical analyzes were carried out with Matlab. The study was approved by the local ethics committee.
Results: The C/D ratio of all patients was calculated 6 months after the transplantation and the patient population was divided into two groups (fast and slow metabolizers) based on a cut-off value of 1.86 ng / ml / mg. A comparison of both groups after 6 and 12 months showed a significantly reduced ΔGFR of the fast metabolizers. After one year, 75.3% of the fast metabolizers had an eGFR <60 ml / min / 1.73 m^2, whereas in the group of slow metabolizers only 45.6% had an eGFR <60ml / min / 1.73 m^2 (p-value < 0,001). There were no significant differences in terms of rejection rate or all-cause mortality.
Conclusion: The C/D ratio appears to correlate with renal function in heart transplant patients. This could be used as a clinical diagnostic tool to identify fast metabolizers and to monitor and treat them more closely with regard to nephropathy.
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S24-05 PK/PD MONITORING IN LCP-TAC TREATED RENAL ALLOGRAFT RECIPIENTS

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Introduction: The pharmacodynamic (PD) monitoring tool – assessing the expression of nuclear factor of activated T-cells (NFAT)-regulated genes - has been established to measure directly the functional effect of calcineurin inhibitors (CNI) in the individual patient. Results on PD monitoring of extended release tacrolimus (LCP-Tac) are presented.
Methods: This pilot study enrolled 44 stable renal transplant patients (22 LCP-Tac, 22 immediate release (IR)- Tac). PK data and NFAT-regulated gene expression (NFAT-RE; IL-2, IFN-y, GM-CSF) was assessed by quantitative real-time PCR in whole blood samples at study start, month 1, 6 and 12.
Results: Baseline characteristics were comparable in both study groups. There was no significant difference in PK and PD data between both groups at study start (all on IR-Tac; Tac C0 7.9±2.3 vs. 7.4±2.2 μg/L; NFAT-RE 30±21 vs. 28±20%). Long-term PK revealed Tac Cmax at 1.5 hours in IR-Tac and at 4 hours in LCP-Tac patients after drug intake. Tac Cmax was significantly lower in LCP-Tac at all time points (month 12 15.8±66 vs. 8.4±2.0 μg/L). NFAT-RE showed a high interindividual variability in IR-Tac and LCP-Tac patients. NFAT-RE correlated inversely with Tac levels in IR- and LCP-Tac with maximum inhibition of NFAT-RE at C1.5 in IR-Tac and at C4 in LCP-Tac. In the

LCP-Tac group NFAT-RE at C1.5 increased from 28±20% on IR-Tac to 50±17% after switch to LCP-Tac, whereas NFAT-RE at C4 was 39 ± 15%. In the IR-Tac groups NFAT-RE at C1.5 was comparable throughout the study. Renal function and blood pressure was stable in all patients. Adverse events were comparable in both groups with 5 infections in the IR-Tac and 6 infections in the LCP-Tac group, and one acute rejection episode in the IR-Tac group.
Conclusion: LCP-Tac inhibits NFAT-regulated gene expression (e.g. IL-2, IFNy, GM-CSF). Maximum inhibition of NFAT-RE in LCP-Tac is at C4 compared to C1.5 in IR-Tac. Therefore, a useful pharmacodynamic marker for LCP-Tac might be the maximum inhibition of NFAT-RE at 4 hours after drug intake. If NFAT-RE at C4 has to same predictive value as in IR-Tac or ciclosporin A has to be evaluated in a larger study.

S25 | ANTIBODY DIAGNOSTICS FOR LIVER AND LUNG TRANSPLANTATION

S25-05 HIGH FREQUENCIES OF DONOR-DERIVED MEMORY T AND NK CELLS IN LUNG TRANSPLANT RECIPIENT BLOOD MAY CONTRIBUTE TO PROTECTION FROM CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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Introduction: After lung transplantation (LuTx), a transient chimerism of donor cells exists in the blood of recipients due to the migration of lymphocytes from the transplanted lung into the periphery. We aimed to characterize the phenotype of donor CD8+ and CD4+ T and NK cells and to investigate whether they might represent tissue-resident memory (TRM) cells.
Methods: Lymphocyte dynamics in recipient blood were determined in 97 lung transplant patients directly (T0), 24 hours (T24) and 3 (wks) weeks after LuTx using flow cytometry with lineage-, tissue-, and donor HLA class I allele-specific mAb. The same makers were used to determine the phenotype of lymphocytes present in organ storage solution (perfusate, n=102), recipient explanted lung parenchyma (n=28) and donor trachea (n=17).
Results: In blood of all recipients, donor-derived $CD4^+$ and $CD8^+$ T and $CD56^{dim}$ NK cells were detected at T0, T24 and 3 wks after LuTx with higher CD69 expression compared to recipient cells (p=0.01 to 0.04). Their memory phenotype was similar to T and NK cells in perfusates. In recipient parenchyma and donor trachea, most $CD69^+$ T and NK cells showed expression of tissue residency markers, i.e. CD103, CD49a and PD-1 with significant enrichment in trachea ($p<0.05$). In contrast, these markers were not found in circulating donor lymphocytes and perfusates, indicating that they represent distinct memory T and NK subsets. Donor T and NK cells showed higher IFN-g production compared to recipient cells upon stimulation ($p<0.05$). Donor T and NK cells had no an impact on the development of PGD 24 h after transplantation. However, patients with high frequencies of donor T cells showed a trend towards a CLAD-free survival 2 years post LuTx.
Conclusion: Our results demonstrate that donor T and NK cells found in the periphery of lung transplant recipients are a distinct subset from circulating lymphocytes and TRM cells present in lung tissue, since they express CD69 but lack expression of other classical TRM markers. They display a higher functional capacity despite the onset of immunosuppression. Donor T cells might be clinically relevant for tolerance induction and long-term survival after transplantation due to their unique features.

S26 | MACHINE PERFUSION OF THORACIC ORGAN

S26-03 COMBINING OXYGENATED COLD PERFUSION WITH NORMOTHERMIC EX-VIVO PERFUSION IMPROVES THE OUTCOME OF DCD PORCINE KIDNEY TRANSPLANTATION

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Introduction: Ex-vivo machine perfusion is a novel preservation technique for the storage and assessment of marginal kidney grafts. Normothermic (NEVKP) as well as hypothermic machine perfusion (HMP) with and without oxygen have been developed in the recent past. All ex-vivo perfusion techniques have advantages and shortcomings. NEVKP reduces cold ischemic injury with opportunities for graft assessment. In contrast, HMP is easier to perform during transportation, but graft assessment is limited. In the current study, we assessed if a combination of oxygenated HMP (oxHMP) followed by a short NEVKP period could combine the advantages of both preservation techniques.
Methods: All pig kidneys were exposed to 30min of warm ischemia followed by 16hr of perfusion. Three ex-vivo perfusion techniques were compared. Kidneys either underwent 16hr NEVKP or were preserved by 16hr oxHMP. The third group was treated with 13hr oxHMP followed by 3hr NEVKP (oxHMP+NEVKP group). After contralateral nephrectomy, grafts were autotransplanted and animals were followed for 8 days. Kidney function and injury markers were compared between groups.
Results: All animals survived the follow-up period. Grafts preserved by NEVKP showed improved function with lower peak serum creatinine (SrCrea) and more rapid recovery compared to the other two groups (peak SrCrea NEVKP vs oxHMP vs oxHMP+NEVKP: 3.7±1.3 mg/dl vs 9±5.5 mg/dl vs 5.6±1.5mg/dl). Groups which received NEVKP peaked sooner, on postoperative day (POD) 1, while the oxHMP group peaked on POD3. The differences in daily SrCrea levels reached significance between NEVKP and oxHMP on POD1- 3 ($p<0.05$) and trended towards a significant difference between NEVKP and oxHMP+-NEVKP on POD1 (p=0.057). On POD3, creatinine clearance was increased in the NEVKP group. Tubular injury and inflammation scores on POD8 were similar in all groups.
Conclusion: Prolonged NEVKP provided superior outcome in DCD kidney transplantation compared to oxHMP and oxHMP+NEVKP. However, the latter was better than HMP alone and represents a practical alternative to NEVKP alone. A combination of oxHMP with end-ischemic NEVKP could be an attractive practical strategy to combine the advantages of both preservation techniques.
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S26-04 COMPOSITION OF EX VIVO LUNG PERFUSION SOLUTIONS AND KINETICS DEFINE DIFFERENTIAL CYTOKINE/CHEMOKINE SECRETION IN A PORCINE CARDIAC ARREST MODEL OF LUNG PRESERVATION

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Introduction: Ex vivo lung perfusion is an innovative technique to evaluate marginal lung organs especially after DCD. Normothermic continuous perfusion should reduce ischemic damage and improve the outcome of lung transplantation. However, the optimal protocol for EVLP has not been defined so far. The aim of our study was to compare cytokine/chemokine concentrations in perfusion solutions using different kinetics and solution compounds of EVLP in a porcine cardiac arrest model and to correlate the inflammatory parameters to oxygenation capacity values.
Methods: Following cardiac arrest and 1h of warm ischemia, lungs were harvested and flushed. Groups were processed as immediate (I-EVLP) 1h cold static preservation (CSP) and delayed (D-EVLP; 9h CSP). D-EVLP lungs were perfused with different solutions: Steen vs. modified Custodiol-N containing

dextran (CD) or dextran/albumin (CDA). Cytokine/chemokine levels were analyzed at baseline (0h), after 1h, 4h using multiplex protein arrays.
Results: Concentrations of TNF-α, IL-6, CXCL8, IFN-γ, IL-1α and IL-1β increased significantly ($p<0.05$) in all four groups. CD-solution contained lower levels of these proteins and IL-2, IL-12, IL-10, IL-4, IL-1RA and IL-18 ($p<0.05$) compared to SteenSolution samples. Protein concentrations correlate negatively with ΔpO_2 values ($p<0.05$). No significant differences could be detected between I- vs. D-EVLP lungs and CD vs.CDA solutions.
Conclusion: In a non-heart beating porcine cardiac arrest model with relevant IRI, lungs were perfused with normothermic EVLP. Longer CSP prior to EVLP did not result in enhanced cytokine secretion, but the first hours of reperfusion seem crucial for tissue damage. CD-solution dampens the cytokine/chemokine secretion probably by iron chelators and, possibly, protecting effects of dextran. Addition of albumin had no further effect on inflammation. Cytokine/chemokine concentrations correlated negatively with the oxygenation capacity, an important parameter for organ acceptance. These finding may help to optimize the *ex vivo* preservation procedure and possibly, more organs could reach the clinically relevant threshold for transplantation, thus, the pool of marginal donor lungs could be enlarged.

S26-05 ASSESSMENT OF LIVER ALLOGRAFT VIABILITY DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION USING THE MS^2 SCORE

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Introduction: Utilization of extended criteria donor organs becomes more and more frequent in order to counteract waitlist mortality. Normothermic machine perfusion (NMP) facilitates checking liver allografts for their viability and has the scope to improve graft quality. A variety of perfusion criteria have been reported previously to assure graft viability. After establishing NMP at University Hospital Muenster we aim to critically evaluate and simplify existing assessment scores and would like to introduce the MS^2 score (Münster machine score).
Methods: In total 15 NMP of liver grafts were performed from 10/19 until 04/20. During NMP portal- and arterial flow, perfusate pH, lactate and glucose levels as well as production of bile, bile viscosity and pH were monitored hourly. A minimum of 4 hours of NMP was local protocol to allow the graft to recover from static cold storage. Perfusate transaminases were monitored at 1, 2, 4, 8, 12 and 16 hours of NMP. Following transplant serum lactate levels, clotting factors and transaminases of the recipient were monitored daily.
Results: Average DRI was 1.84 despite short average cold ischemia time of 6.5 hours. Average NMP lasted 12 hours. Median recipient MELD was 26. All transplants were successful, there was neither PNF nor EAD beyond postoperative day 3, except for 2 cases (13%) with elevated bilirubin levels for >7 days. Using other reported viability variables such as transaminases >6000 U/l and perfusate pH<7.2 we would have excluded 6 livers. Applying the Cambridge glucose metabolism criteria 4 additional grafts would have been excluded. Relying on perfusate lactate level (<3 mmol/l @ 4 h), arterial flow (>150 ml/min or >20% of total perfusion volume) and production of viscous bile was sufficient for viability assessment. The presented simplified MS^2 score seems to be sufficient for viability testing livers on NMP including a significant proportion of grafts which elsewhere would have been excluded.
Conclusion: The MS^2 score provides a simple and therefore ideal tool for viability assessment of livers on NMP. Previously reported viability criteria might have been chosen too carefully and would have excluded significant portion of functioning liver allografts.

S26-06 RELEVANCE OF THE SOLUBLE UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) IN A RECIPIENT AND LIVING DONOR KIDNEY TRANSPLANT COHORT

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Introduction: The soluble urokinase-type plasminogen activator receptor (suPAR) and its membrane bound form uPAR are signaling proteins of the Ly6/alpha-neurotoxin family. In the kidney, suPAR binds to and activates αvβ3 integrin on the podocyte membrane (1). Thereby it contributes to podocyte foot process effacement and disrupted glomerular barrier function (2). Its role for allograft function or transplant specific outcomes needs further clarification and its meaning for living kidney donors is completely unknown yet. We prospectively investigated the prognostic relevance of suPAR before and one year after Tx or kidney donation.
Methods: We included 100 consented patients who received a kidney transplant at our transplant center between 2013 and 2015. In addition, 51 living donors were analyzed. Plasma concentration of suPAR was measured by uPAR ELISA assay.
Results: In patients who received a living donation (LD), pre-transplant suPAR levels were significantly lower compared to those receiving a cadaveric donation (CD) (suPAR 7619±3844 vs. 10043±4053 pg/ml, p=0.003). suPAR levels significantly declined in LD and CD recipients after Tx (8665±4099 before Tx vs. 4540±2449 pg/ml one year after Tx), (n=100, $p<0.001$) without a detectable difference between LD and CD recipients. Higher suPAR levels in recipients one year after Tx were associated with a higher eGFR-loss in the following three years (n=82, p=0.021). In donors, higher suPAR levels prior to nephrectomy were associated with a more pronounced eGFR loss within the following three years (n=42, p=0.011). Despite a significant decline in kidney function (eGFR: −21.3±9.3 ml/min/1.73 m^2) of donors after LD (pre-LD: 88.2±14.85 vs. 66.9±14.58 ml/min/1.73 m^2 at 1-year after LD ($p<0.001$)), there was no significant difference in the donors' suPAR level before and one year after removal of one kidney (3873±2575 vs. 4248±2021 pg/ml, n=44, p=0.212).
Conclusion: suPAR might rather be a consequence of than a cause for kidney disease. After Tx, suPAR levels drop significantly to donors' niveau. Secondly, it could serve as a marker for kidney disease but not for kidney function, as it does not significantly increase after removal of one kidney in living donors.
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