EXPERIMENTAL

P01 IRON CHELATION WITH DEFEROXAMINE ALLEVIATES ISCHEMIA REPERFUSION INJURY IN A STRICTLY DOSE DEPENDENT MANNER

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Background: Reactive oxygen species formation catalyzed by chelatable, redox-active iron represents an important contributor to ischemia reperfusion injury (IRI) in the setting of solid organ transplantation. In vitro data suggest that iron chelation during organ preservation might offer a promising approach to alleviate IRI.
Methods: To comprehensively investigate the effects of the iron chelator deferoxamine (DFO) in an in vivo IRI model, hearts from C57BL/6 donors were perfused and stored with histidine-tryptophan-ketogluterate (HTK) solution containing rising concentrations of DFO (50–1000 μM). After 9 h of cold ischemia, syngeneic cardiac transplantation (HTx) was performed.
Results: As illustrated by a cumulative histological damage score heart grafts solely perfused with HTK solution displayed signs of severe IRI 48 h post-transplant. While addition of 50 μM DFO could not alleviate the extent of the injury (HTK: 7.3 ± 0.6 vs. HTK+DFO50: 7.1 ± 0.8; $p = 0.8$) treatment with 100 μM of DFO resulted in a significant improvement of the observed damage (HTK+DFO100: 2.8 ± 0.6; $p < 0.001$). In contrast to prior in vitro studies, doubling of the applied dose failed to further improve IRI but the protective effect diminished (HTK+DFO200: 4.6 ± 0.6) and showed a plateau at higher dosages (HTK+DFO500: 4.7 ± 0.4; HTK+DFO600: 4.7 ± 0.7; $p < 0.05$ respectively). Importantly, further dose escalation to 700 μM and 1000 μM annulled the protective effects of DFO (HTK+DFO700: 6.0 ± 1.08; $p = 0.2$ and HTK+DFO1000: 7.0 ± 0.6; $p = 0.5$), potentially due to the resulting toxicity at these concentrations.
Conclusion: Iron chelation during organ preservation has the potential to significantly alleviate IRI following solid organ transplantation. However, regarding the strict dose dependency in the murine model, further kinetic studies are required to better characterize the mechanisms by which DFO exerts its beneficial effect.

P02 CHANGES IN FREQUENCY OF ANTIGEN PRESENTING CELLS AND SURFACE MARKER EXPRESSION AFTER MANIPULATION WITH IL-2-COMPLEXES

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Introduction: The use of Interleukin-2 (IL-2) bound to a specific antibody against IL-2 (IL-2cplx) allows the selective expansion of regulatory T cells (Tregs) and has been demonstrated to prolong allograft survival. Here, under IL-2cplx treatment, we focused on the frequency of Antigen Presenting Cells (APC) and possible changes in the expression of markers relevant for immune response activation.
Methods: C57BL/6 mice received intraperitoneal injections of either PBS (control) or IL-2cplx (1 μg IL2/5 μg anti-IL-2) on three consecutive days and were sacrificed on day 5. We used flow-cytometric analysis to investigate the frequency of Tregs and APCs focusing on the expression of CD80, CD86, PDL-1 and MHC-class-II on $CD11^+$ Dendritic cells (DCs) in samples taken from spleen.
Results: Beside a significant increase in Tregs (17.88% vs. 4.3% $p < 0.001$) and CD11c+DCs (2.01% vs. 0.94% $p = 0.005$; vs. naïve), treatment with IL-2cplx led to a significant higher expression of MHC-class-II on CD11c+DCs (82.9% vs. 75.35% $p = 0.009$; vs. naïve). Beyond that, within the DC compartment we observed significantly lower expression of costimulatory molecules CD80 and CD86 (16.4% vs. 22.8% $p = 0.02$ and 29.8% vs. 34% $p = 0.09$; vs. naïve).
Conclusion: Our data demonstrate that treatment with IL-2cplx not only leads to significant Treg expansion but also to changes in APC frequencies and surface marker expression. We assume that this could cause a possible impaired T cell effector function and memory cell formation. These data highlight potential mechanisms mediated by APCs and T cells that may have implications for immune cell modulation protocols for in human organ transplantation.

P03 P66SHC: A DRUGGABLE TARGET IN THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY (IRI)?

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Background: Excessive production of reactive oxygen species (ROS) has been causally linked to the development of ischemia/reperfusion injury (IRI) during solid organ transplantation. Antioxidants so far failed in the clinic. p66Shc is unique among ROS producing systems as its knockout did not affect normal signaling and thus survival while it prevented pathophysiological conditions caused by excessive ROS production. In our work we are attempting to devise strategies to target signaling pathways, which control the activation of ROS producing systems for the prevention of IRI.
Material and Methods: Various cellular models and conditions were uses to simulate ischemia-reperfusion in vitro. p66Shc regulation by signaling pathways was addressed by using immunoblot analyses, mass spectrometry, mutagenesis and reconstitution assays in wildtype and p66Shc-deficient cells.
Results: p66Shc, the longest form of the ShcA adaptor proteins normally resides in the cytoplasm. Previous work suggested that the activation of the pro-oxidant and pro-death function of p66Shc required phosphorylation on serine 36 (S36) followed by mitochondrial import and PKCβ has been proposed as S36 kinase. Due to the lack of inhibitors of its oxidoreductase function we pursue a strategy to inhibit p66Shc by interfering with its upstream activation. To this end we initiated a detailed analysis of the signaling interaction controlling p66Shc activation and function under cellular stress. In our work we could confirm the requirement of PKCβ for ROS production and cell death but not for p66ShcS36 phosphorylation. Our search for a bona fide S36 kinase lead to JNK1/2, whose involvement was confirmed through the use of inhibitors and JNK1/2-deficient cells. Moreover, expression of a S36E mutant in p66Shc-deficient cells restored ROS production under the stress conditions tested here. Additionally, we identified S139, T206 and S213 as critical PKCβ target sites regulating the pro-oxidant and pro-death function of p66Shc.
Conclusions: In our work we established the conditions for the inhibition of the oxidoreductase p66Shc, a main contributor to pro-oxidant damage during ischemia and reperfusion. Both, JNK1/2 and PKCβ, are normally activated under cellular stress and targeting them may provide a novel therapeutic approach to prevent IRI and other diseases associated with excessive ROS production.

P04 GLUCAGON-LIKE PEPTIDE 1 RECEPTOR SIGNALING AMELIORATES RENAL ISCHEMIA/REPERFUSION INJURY

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Introduction: Besides a crucial role in blood glucose homeostasis, Glucagon-like peptide 1 receptor (GLP1-R) signaling has been found to hold additional functions, including antiinflammatory effects. Renal ischemia/reperfusion injury (IRI) is unavoidable in renal transplantation, thus influencing early and late outcome. Since kidneys from non-heartbeating and extended criteria donors are increasingly transplanted due to organ shortage, this study aimed to evaluate the role of GLP-1R signaling in a murine model of renal ischemia/reperfusion injury.
Methods: All mice were anesthetized, kept at 37°C, and both renal pedicles were occluded using micro clamps for 25 minutes with subsequent 24 h reperfusion. Starting seven days before IRI, C57Bl/6J mice were treated with the GLP-1R agonist Liraglutide. Mice received either 200 μg/kg BW Liraglutide

or vehicle by daily intraperitoneal injections. In a second set of experiments, GLP-1R knock-out (KO) and wildtype (WT) mice on C57Bl/6J background were used and subjected to renal IRI experiments.
Results: WT mice treated with daily Liraglutide displayed significantly decreased serum-urea, serum lipocalin-2 and BUN levels as compared to vehicle-treated mice 24 h after renal IRI. Increased numbers of macrophages infiltrated kidneys of Liraglutide-treated mice as compared to controls after 24 h of reperfusion. These macrophages were further characterized to have an alternatively activated M2 phenotype. Conversely, GLP-1R KO mice showed increased serum-urea values when compared to WT mice 24 h after renal IRI.
Conclusion: Promotion of GLP-1R signaling using a GLP-1R agonist leads to improvement of renal IRI. Our data suggest a protective role of GLP-1R signaling via propagation of anti-inflammatory M2 macrophages.

HEART

P05 CORONARY ANGIOGRAPHY OF POTENTIAL CARDIAC DONORS INCREASES CARDIAC TRANSPLANTATION RATES

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Purpose: Donor age has increased dramatically in Europe. There exist concerns about transmission of coronary artery disease (CAD) in older donors, with associated complications like primary graft failure and graftvasculopathy. Donor coronary angiography (DCA) can detect CAD but is not regularly used in all donors. The aim of this study was to analyse if donor angiography has an impact on heart transplant rates.
Methods: Between 2004 and 2016 all donor heart offers within Eurotransplant were analysed for DCA use and transplantation rates. DCA rate was calculated and compared for different donor risk variabels: age, sex, diabetes (DM), hypertension (HT), smoking history (SH) and body mass index >30 (BMI). Influence of donor risk factors on DCA results were analysed. The likelihood of transplantation of donors with and without DCA was compared in the overall donor population as well as within risk groups. Multiple logistic regression models were created to analyse the influence donor risk factors on DCA- rates, -outcome and transplantation rates. P-value of <0.05 was defined as statistical significant.
Results: A total of 12565 donor hearts were offered during the study period. In 2319 (18.5%) DCA's were performed. 107 DCA's were excluded due to unclear results. Median donor age was 45 (31–53) years, 54.4% were male. 3.4% of donors had DM, 20.5% HT, 44.4% SH and 10.0% had a BMI ≥30. Donor risk variables had a significant impact on DCA use: Age (10 year increments (10a): $p < 0.0001$, OR:2.797), DM ($p < 0.0001$,OR:1.811), HT ($p < 0.0001$, OR:1.349), SH ($p < 0.0001$,OR:1.859), BMI ($p = 0.01$,OR:1.240), male ($p = 0.0002$,OR:1.235). CAD was associated with donor age (10a: $p < 0.0001$,OR:1.545), HT ($p = 0.0006$,OR:1.425), SH ($p < 0.0001$,OR: 1.903), male ($p < 0.0001$,OR:2.247). Transplant rates were significantly higher in donors with normal DCA result (compared to no DCA performed: $p < 0.0001$, OR:2.612), whereas other independent risk factors for transplantation were: Age (10a: $p < 0.0001$, OR 0.775), DM ($p = 0.0019$,OR:0.689), HT ($p = 0.002$, OR:0.84), male ($p < 0.0001$,OR:0.738) and CAD detected by DCA ($p < 0.0001$,OR:0.832).
Conclusion: DCA is used more often in donors with potential CAD risk factors. Donor CAD is associated with known risk factors. However, normal DCA results are associated with higher transplant rates independent of CAD risk factors. Higher use of DCA might increase transplant rates, especially in donors with CAD risk.

P06 RISE AND FALL OF THE MACHINE: HIGH URGENT HEART TRANSPLANTATION DUE TO OUTFLOW GRAFT TWISTING IN HEARTMATE 3 DURING FOLLOW UP

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The fully magnetically levitated Heartmate 3 received market approval in Europe in 2015 based on excellent results in the CE mark trial. Despite initial positive results concerning pump thrombosis or pump failure, Abbott had to send out a recall on the device due to malfunction of the outflow graft assembly causing graft twisting or occlusion in April 2018
Case report: We present a case of a 47-year old male who suffered from ischemic cardiomyopathy and received a Heartmate 3 as bridge to transplant due to massive pulmonary hypertension in November 2015. LVAD implantation was uneventful and the patient was seen in the outpatient clinic on a regular base. 8 months after device implantation the patient was readmitted to the hospital due to low flow alarms. Transthoracic echocardiography was satisfying with adequate LV unloading, but blood word revealed elevated hemolysis parameters (LDH 427 U/L). As low flow alarms could not be resolved despite aggravation of anticoagulation treatment, thoracic CT angiogram was performed and showed massive thrombosis of the outflow graft. Due to this life threatening device complication and the impaired clinical status of the patient, a high urgency request for heart transplantation was filed and immediately accepted. The patient went into progressive heart failure during waiting time and finally was transplanted after 9 days and received an excellent organ. Device explanation showed twisting of the outflow graft cannula at the proximal portion. Despite intravenous argatroban therapy residual thrombotic material could still be identified inside the graft. The clinical course post transplantation was uneventful, the patient could be discharged after 30 days and had perfect two-year follow up outcome.
Summary: We report our clinical experience with one patient suffering from outflow graft twisting resulting in thrombosis and pump malfunction. In selected patients with LVAD complications, heart transplantation remains a life-saving procedure with excellent outcome.

P07 TREATMENT OF THERAPY-RESISTANT HYPERLIPIDAEMIA AFTER HEART TRANSPLANT WITH PCSK9-INHIBITORS

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Introduction: Hyperlipidaemia is a major factor in the development of graft vasculopathy (GVP) after heart transplant. The incidence of hyperlipidaemia in heart transplant (HTX) patients under immunosuppressive therapy is 74% in the first year, and 91% in the first five years. Lipid-lowering therapy with statins presents a great challenge due to interactions and adverse effects. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have already proven very effective in high-risk cardiovascular patients. In our centre, PCSK9-inhibitors have been administered to selected HTX-patients, in which the target LDL-Cholesterol of 100 mg/dL could not be reached with reasonable doses of statins and/or Etizimib.
Materials and Methods: In the period 02/2017 to 12/2017, 13 adult HTX-patients (age 60.4 ± 10.9, 30.8% female) were selected. The patients were 54.3 ± 40.1 months post-HTX. The selected patients were evaluated together in the lipid clinic (licenced for PCSK9-inhibitors). Therapy was initiated with Alirocumab 75 mg. Statin-therapy was changed and appropriately documented when changes in lipid-parameters and/or adverse effects occurred. In order to evaluate incidence and prevalence of myopathy and hepatotoxicity, CK and liver enzymes and were measured 1, 3 and 6 months post conversion. Analysis of effectiveness were conducted by measuring blood lipids (LDL-C, HDL, total Cholesterol, Triglycerides, and LP(a)).
Results: Total Cholesterol (228.9 ± 37.4 vs. 136.1 ± 42.5 mg/dL; $p < 0.001$), LDL-Cholesterol (140.4 ± 27.6 vs. 53.6 ± 24.1 mg/dL; $p < 0.001$), and Lipoprotein (a) (69.7 ± 71.9 vs. 46.4 ± 54.8 mg/dL; $p = 0.002$) showed significantly lower levels after conversion and stayed significantly low until the end of the observation period. Triglycerides (165.9 ± 45.9 vs.157.8 ± 75.5 mg/dL, p=n.s.) and HDL-Cholesterol (55.2 ± 11.6 vs. 53.2 ± 19.6 mg/dL; p=n.s.) did not change. Prevalence of CK and rises in transaminases did not change (CK46.2%, GPT 7.7%, GOT:7.7%, GGT:23.1%). Adverse effects associated with PCSK9-inhibitors (nervous system, pain symptoms) occurred in none of the treated patients; none of the treated patients had to terminate therapy.
Discussion: Therapy with PCSK9-inhibitors (Alirocumab) constitutes an effective and safe option in therapy of hyperlipidaemia after heart transplant. Under treatment liver and kidney parameters stayed stable, while a significant reduction of lipid levels could be achieved. To evaluate the long-term effects of PCSK9-Inhibitors longer observation period is necessary.

P08 THE ROLE OF HLA-EPITOPES IN HEART TRANSPLANTATION

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Background: HLA epitope mismatching has been shown to adversely affect outcomes after kidney transplantation. The aim of this study was to evaluate the role of molecular-level HLA matching on HTX post-transplant graft survival, rejection and cardiac allograft vasculopathy (CAV).
Methods: We retrospectively analyzed all primary cardiac transplant recipients between 01/1984 – 06/2016. 1,167 patients fulfilled inclusion criteria with HLA typing information available for donor and recipient. In 312 pairs high resolution HLA typing at split antigen level was available for AB and DR. We used the HLAMatchmaker algorithm (version 02.1) to calculate antibody verified amino acid differences (epitope mismatch load (epMM)) between donor and recipient HLA type. In order to group patients in high and low epMM, we split the collective at the respective median. Kaplan Meier analyses with log-rank tests were used to compare outcomes between groups. A p-value of <0.05 was defined as significant.
Results: Patients with a DR epMM load below the median (<5) had a superior 1-year graft survival compared to patients above the median ($p = 0.003$). AB epMM showed no impact (median: 8; $p = 0.63$). Patients with available split level information additionally showed in long-term follow-up (median: 8 years, IQR: 3–15 y): a survival benefit for a DR epMM below the median ($p = 0.03$), no impact of AB epMM on survival and a lower cumulative incidence of rejection for an AB ($p < 0.001$) and DR ($p = 0.008$) epMM below the median. The latter was confirmed via multivariable cox proportional hazards model taking into account HTX eras and immunosuppression regimen (Tac vs. CyA) for AB (HR 1.63; 95% CI 1.23–2.14; $p < 0.001$) and DR (HR 1.37; 95% CI 1.12–1.67; $p = 0.002$). There was no impact on the development of CAV.
Conclusion: HLA matching at the epitope level is a useful tool for risk stratification after heart transplantation and might open up a new pathway into precision medicine in solid organ transplantation.

LIVER

P09 SURGERY VERSUS ENDOSCOPY FOR ISCHEMIC TYPE BILIARY LESIONS LATE AFTER LIVER TRANSPLANTATION

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Background: Incidence of late biliary complications after liver transplantation is rising with acceptence of marginal grafts (DCD, ECD). Aim of this study was to compare surgical versus endoscopic treatment for late non-anastomotic/ischemic biliary lesions after liver transplantation.
Methods: A retrospective review of 1348 consecutive patients, who underwent liver transplantation between 1989 and 2009 was performed. 1188 patients were included in this study. Management strategies (endoscopic, surgical or combined approach) were evaluated for treatment success as well as patient survival.
Results: Ischemic type biliary lesions (ITBL) were identified in 67/1188 patients. 50 patients received primary endoscopic treatment (48% of whom were successful), 17 patients received primary surgical treatment (71% of whom were successful). 24 patients needed referral to surgery after endoscopy.. Overall 41 patients were in need of a surgical approach, which was successful in 36 patients. 7 patients were retransplanted.
Conclusion: Our data suggest, that while endoscopy is established as gold standard in treatment of biliary complications, there should be careful evaluation for a primarily surgical approach in patients with late ITBL

P10 BRIDGING HCC PATIENTS BEFORE LIVER TRANSPLANTATION

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Background: It is current practice, that HCC patients with listed for liver transplantation should receive locoregional treatment if suspected waiting time for transplantation is longer than six months, even in absence of prospective randomized data. Aim of this study was the comparision of single versus multimodality locoregional treatment strategies on outcomes after liver transplantation.
Methods: This is a retrospective analysis of 150 HCC patients listed for liver transplantation at our center between 2004 and 2011. Outcomes were analyzed according to mRECIST in relation to intention to treat and overall survival after liver transplantation.
Results: Overall 92 patients (63%) were transplanted in this cohort. The intention to treat 1-, 3-, 5- year waiting list survival was 80, 59, and 50% respectively. In RFA and TACE based regimens rates of transplanted patients were comparable (69 vs. 58%, p = ns). No difference was seen in overall survival after liver transplantation when comparing TACE and RFA based regimen. Patients receiving multimodality loco regional therapy had lower overall survival after transplantation ($p = 0.05$)
Conclusion: TACE and RFA based regimen showed equal outcomes in terms transplantation rate, tumor response and post-transplant survival. Patients in need of more than one treatment modality might identify a cohort with poorer post-transplant survival.

P11 HIGH EXPRESSION OF THE MAJOR HISTOCOMPATIBILITY CLASS I-RELATED CHAIN MOLECULE A (MICA) IN ZERO HOUR BIOPSIES PREDICTS IMPROVED GRAFT SURVIVAL AFTER LIVER TRANSPLANTATION

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Background: In search for novel biomarkers to assess graft quality, we investigated whether defined candidate genes are predictive for outcome after liver transplantation (LT). METHODS: Zero-hour liver biopsies were obtained from 88 LT patients. Gene expression was analysed and correlated with clinical parameters, including the Eurotransplant Donor-Risk-Index (ET-DRI) as well as short and long-term outcomes.
Results: Among the markers studied (MICA, NKG2D, CCL19, DNAM1, HLADRB, Leptin), the mRNA expression of the cytotoxicity receptor NKG2D significantly correlated with a body mass index >30. However, its ligand MICA was significantly upregulated in patients at advanced age of >55 yrs. Whereas both the calculated ET-DRI and donor BMI had either a poor or no predictive value concerning serum levels indicative for liver function (ALT, AST, bilirubin, GGT) after 6 months, chronological donor age was only predictive for serum bilirubin (AUC=0.67). In contrast, MICA demonstrated a high predictive value for serum liver function parameters including ALT (0.8), AST (0.78) as well as bilirubin (0.63) and GGT (0.66) after 6 months post LT. Likewise, after 24 months, MICA still showed a high AUC for ALT (0.71), AST (0.73) and GGT (0.75) but not for serum bilirubin (0.5). Importantly, high expression of MICA was detected to be significantly associated with prolonged graft survival ($p = 0.024$; log rank test) after 10 years of observation.
Conclusion: Cold as well as warm liver preservation systems now allow a longer time frame for the simultaneous evaluation of biomarkers to diagnose graft quality. Given the observed correlation with short and long-term graft function, we suggest MICA as a biomarker for zero-hour biopsy assessment.

P12 C-REACTIVE PROTEIN IS AN INDEPENDENT PREDICTOR FOR RECURRENCE IN HCC PATIENTS UNDERGOING LIVER TRANSPLANTATION

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Background: C-reactive protein (CRP) is an independent prognostic factor for overall survival (OS) and recurrence in hepatocellular carcinoma (HCC) patients treated with resection or non-surgical treatment. The aim of this study was to investigate if CRP (≥1 vs. <1 mg/dL) is associated with OS or recurrence in HCC patients undergoing liver transplantation (LT).
Methods: A retrospective analysis of a cohort of HCC patients (≥ 18 years) who received LT at the Medical University of Vienna between 1997 and 2014 was conducted. Both univariate (log-rank test, Kaplan-Meier-plots) and multivariate analysis (Cox proportional hazards model) were employed. Variables with a p-value <0.1 were included into multivariate analysis.

Results: Of 216 patients included, 189 (87.5%) were male and 27 (12.5%) were female. One-hundred and twenty-eight patients (59.3%) were within Milan criteria, 42 patients (19.5%) had vascular invasion on explant histology. Median AFP was 8.20 IU/mL and 70 patients (32.4%) had a CRP $\geq$ 1 mg/dL. On multivariate analysis, elevated CRP ($\geq$ 1 mg/dL) was an independent predictor for higher recurrence with a 5-year recurrence rate of 27.4% (CRP $\geq$ 1 mg/dL) vs. 16.4% (CRP < 1 mg/dL) (HR 2.33; 95% CI 1.13–4.83; p = 0.022). Higher number of nodules, large tumor size, the presence of vascular invasion, Milan out and high AFP level were predictors for high recurrence rate as well. There was no significant difference in OS in patients with normal vs. elevated CRP.
Conclusion: CRP was independently associated with a higher recurrence rate in patients who underwent LT for HCC and may be a marker for more aggressive tumor biology. Our results suggest that patients with elevated CRP before liver transplantation should undergo a tighter follow-up for early detection of recurrence. Prospective validation is needed.

P13 THE SURGICALLY COMPLEX LIVER RECIPIENT IN THE ERA OF NORMOTHERMIC MACHINE PERFUSION: A CASE REPORT

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Introduction: Normothermic machine perfusion (NMP) has evolved as a further option to safely increase the donor pool. So far, the main indications are preservation and evaluation of marginal donor livers, as well as logistic reasons. We herein present a case, were NMP was applied to ensure liver transplantation in a surgically highest-risk patient.
Methods and Results: The 34 year od patient was referred to our center due to recurring massive gastrointestinal bleedings from a varix from the cholezystojejunostomy performed in his childhood due to biliary atresia. Since bleedings were neither interventionally nor surgically controllable, and up to 33 red-packed cells/24 h were required to maintain hemodynamic stability, the patient was accepted for a HU liver-transplant.

As a liver graft was accepted, NMP was used to enable the surgical team to safely perform the highest-risk surgical procedure. Parallel to initiation of anesthesia, NMP was set up and the liver placed on the device. Perfusion paramters were regular over the entire course, displayed by adequate lowering of lactate-levels and maintenance of physiological pH-values Meanwhile, a non-stressful exploration of the abdomen was performed. Due to a portal vein thrombosis grade IV a large perigastral varix was isolated for later portal anastomosis. Total time until hepatectomy was 7 h 35 min, anastomosis time was 48 min and total duration of the procedure was 12 h 17 min. Total preservation-time was 12 h 36 min (6 h 42 min CIT, 5 h 52 min NMP). Anesthesiological course was uneventfull and the patient was hemodynamically stable over the entire procedure. Initial liver function was good without any immunological problems. No further episodes of GI-bleedings occured. An infection of unknown focus was succesfully treated with antibiotics and the patient was released in good clinical condition on the 22nd pod.
Conclusion: To our knowledge this ist he first case were NMP was successfully applied to manage the surgically complex recipient. Hence, in selected cases NMP may eventually enable safe liver transplantation in potential recipients, were a time-consuming hepatectomy is expected.

P14 HYPONATREMIA PRIOR TO LIVER TRANSPLANTATION IS NOT ASSOCIATED WITH POST-OPERATIVE ENCEPHALOPATHY

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Background: Hyponatremia occurs in about 15% of patients with end-stage liver disease with associated waiting list mortality; however, its impact on post-operative encephalopathy and survival after transplantation remains unclear.
Methods: Patients with pre-operative hyponatremia, defined as a serum sodium (SNa) < 130 mmol/L and a SNa shift within the first 24 hours following liver transplantation, have been evaluated between January 2004 and December 2016 retrospectively. Liver disease, hepatic encephalopathy, intra-operative/peri-operative SNa levels and shift of SNa were compared between patients with and without neurological symptoms.
Results: While 8.1% (16/198) of patients presented with pre-operative hyponatremia a rapid increase of SNa (ΔNa > 10 mmol/L) was observed in 16.7% of patients. There were 12 patients (6.1%) with neurological symptoms and 1 patient (0.5%) developed central pontine myelinolysis (CPM) with a ΔNa > 12 mmol/L; however, both hyponatremia and rapid increase of SNa did not have any impact on neurological symptoms (p > 0.1). Further there was no significant correlation between neurological symptoms and both hyponatremia and rapid increase of SNa.
Conclusion: Hyponatremia is not a contraindication for liver transplantation; however, a rapid increase of SNa shall be omitted to prevent CPM. Thus a careful monitoring of SNa is a prerequisite for the patients' safety during liver transplantation.

P15 PLATELET SEQUESTRATION AND PLATELET INDUCED SINUSOIDAL ENDOTHELIAL CELL INJURY IN THE LIVER CAN BE PREVENTED BY PRE-TRANSPLANT NORMOTHERMIC EX VIVO LIVER PERFUSION

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Background: Normothermic ex vivo liver perfusion (NEVLP) is a rapidly evolving method used as alternative to static cold storage (SCS) for graft-preservation. The aim of this study was to evaluate the impact of NEVLP on platelet-aggregation and platelet-mediated sinusoidal endothelial cell (SEC) injury.
Method: Pig liver transplantation (LT) was performed using heart-beating donor (HBD) and donation after circulatory death (DCD) livers (30 min warm ischemia) subjected to 8 hrs SCS (SCS-group) or NEVLP (NEVLP-group, n = 5/group). Liver biopsies obtained 3 hrs post-LT were stained for platelet-specific CD61. Circulatory TGF-β and platelet-specific micro-particles (PMPs) were analysed. SEC-integrity was determined by CD31-staining and measurement of Hyaluronic Acid (HA). Liver enzymes, platelet-counts, prothrombin time and hemoglobin were measured during a 4-day survival-period.
Results: HBD- and DCD-NEVLP-groups showed significantly lower AST-levels on POD1 and POD2 compared to the SCS groups. Platelet-count recovery was significantly faster in the NEVLP groups within 24 hrs after transplantation. Additionally, intrahepatic platelet-sequestration and aggregation was significantly higher in the SCS-groups (# of clumps; HBD-groups: p = 0.039 and DCD-groups: p = 0.021, respectively). TGF-ß levels were significantly higher in both SCS-groups postoperatively. There was a trend towards higher levels of PMPs on POD1 in the SCS-groups vs. the NEVLP-groups (fold increase: HBD-livers = 3.26 $\pm$ 0.48 vs. 2.37 $\pm$ 1.34, 30'DCD-livers = 7.61 $\pm$ 7.46 vs. 5.6 $\pm$ 7.3). Platelet aggregation correlated with SEC injury, evaluated by scoring the CD31-staining. Consistently, HA levels were significantly higher in SCS-groups vs. NEVLP-groups 3 hrs&24 hrs post-LT (p = 0.007 and p = 0.001, respectively).
Conclusion: NEVLP allows a faster recovery of the platelet count after LT and protects the liver from intrahepatic platelet aggregation and platelet-induced SEC injury.

P16 ACELLULAR GROWTH RETARDATION ABILITY (AGRA) PREDICTS THE OCCURRENCE OF SEVERE BACTERIAL INFECTIONS IN CIRRHOSIS

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Background: Patients with liver cirrhosis often suffer from severe infections which are commonly accompanied by life-threatening complications. Severe infections remain a serious threat to patients even after liver transplantation. A reliable method to predict the occurrence of those infections and therefore improve the chance to prevent them is currently missing.

Serum as many other tissues and body fluids is rich in antimicrobial peptides and proteins that can kill or inhibit the growth of pathogens, including a wide range of bacteria. We developed a functional biomarker, Acellular Growth Retardation Ability (AGRA), that quantifies the antimicrobial activity of serum to determine the infection risk of patients with liver cirrhosis, and describe its possible applications in liver disease.

Method: AGRA was used to quantify the growth of bacteria challenged by serum of patients with liver cirrhosis (n = 146) or pre-cirrhotic chronic hepatitis C patients (n = 81) or healthy controls (n = 42). Part of the patients with cirrhosis of various aetiologies (n = 101) were followed-up for a median time of 36 months to determine the time to occurrence of the first severe infection after inclusion. The remaining patients with chronic hepatitis C infection with and without cirrhosis underwent antiviral therapy and AGRA was monitored throughout its course.
Results: AGRA successfully predicted the occurrence of severe infections in patients with liver cirrhosis (AUROC [95%CI]: 0.8[0.7; 0.9]; $p < 0.001$). Patients with hepatitis C related cirrhosis showed significantly impaired AGRA compared to patients with alcoholic pathogenesis ($p < 0.001$) or other types of aetiologies ($p < 0.001$). Chronic hepatitis C patients also showed impaired AGRA in absence of cirrhosis compared to healthy controls ($p < 0.001$). After antiviral therapy AGRA significantly improved in patients with ($p < 0.001$) and without cirrhosis ($p = 0.001$).
Conclusion: AGRA can be used to predict severe infection in cirrhosis and could also track treatment related improvements of the humoral immune system, as it is shown here with the example of antiviral therapy. This highlights the potential role of AGRA in transplantation medicine: by predicting severe infections, patients at risk can receive preventive therapy and the mortality on the waiting list and possibly after liver transplantation can be reduced.

P17 PLATELETS AND PLATELET GRANULA DERIVED GROWTH FACTORS IN LIVER TRANSPLANTATION

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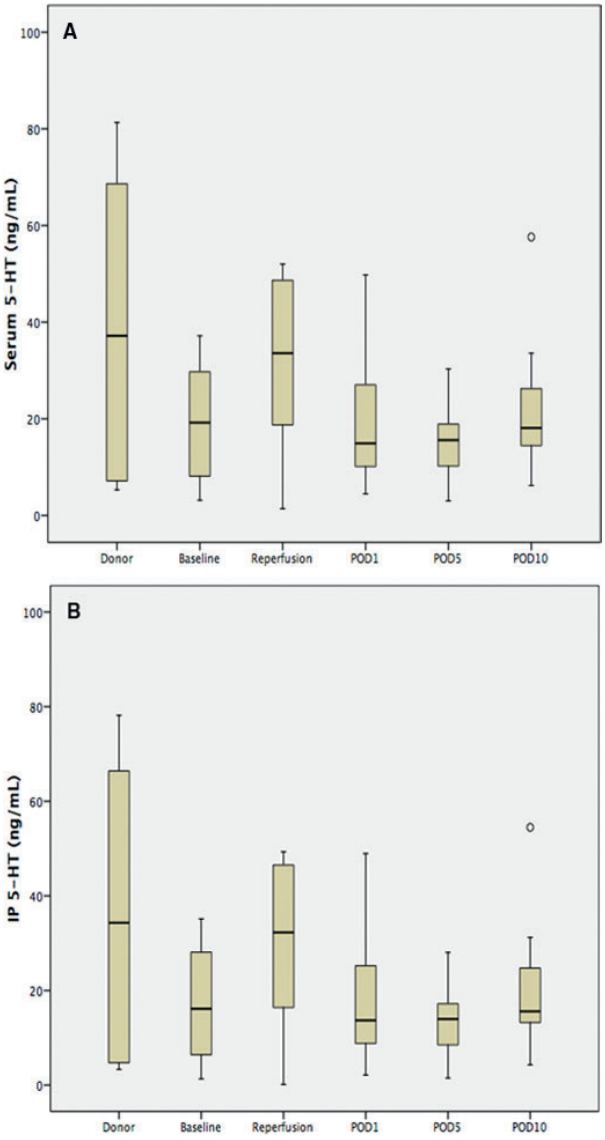
Background: Multiple factors have been described to better classify organ quality in liver transplantation. In the oncological setting thrombocytes and their tissue hormones have been identified as significant factors. Especially intra platelet granula seem to have a positive effect on liver regeneration. If a similar effect can be seen in liver transplantation has not been investigated yet and is aim of this study.
Method: To investigate the serotonin levels of the thrombocytes blood draws were taken form the donor before organ harvest and from the recipient at 5 different time points (pre TX, 30 min after reperfusion, day 1/5/10). Samples were analyzed by serotonin ELISA. Intracellular concentration of Serotonin were calculated by subtraction of plasma from serum levels. For outcome Olthoff-Criteria, re-transplantation and survival after 90 days were analyzed.
Results: In total 12 liver transplant recipients and their donors analyzed. Plasma-Serotonin-levels presented expectably low and showed no significant dynamic during the perioperative course (recipient: 2.18 ug/mL, SD 0.64 ug/mL). Serotonin-Levels in the serum und intracellular were significantly lower compared to a historic oncological cohort. Donor levels were significantly higher than the recipient levels. Serum donor 38.50 ± 29.55 ng/mL vs. recipient 34.30 ± 43.64 ng/mL, intracellular donor 36.32 ± 29.48 ng/mL vs. recipient 32.11 ± 43.25 ng/mL, both $p < 0.01$. Postoperatively a significant decrease was investigated, which can be seen even 19 days postoperatively. Figure 1.
Conclusion: Thrombocyte regeneration seems to last longer in the transplant than liver resection setting. Significantly lower serum- und intracellular Serotonin levels of recipients represent their grade of endstage liver cirrhosis. Figure 1.



P18 IMPACT OF MELD-NA COURSE (DELTA MELD-NA) ON OUTCOME AFTER LIVER TRANSPLANTATION

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Background: Currently, MELD Score listing is state of the art for liver transplant recipients. Our department could show by our own data and confirmed by an ET- cohort that dynamic MELD deterioration (Delta MELD) during waiting time has a significant impact on postoperative survival. Aim of this study was to analyze the risk prediction of posttransplant survival by adding recipient Sodium values to Delta MELD (Delta MELD-Na).
Method: More than 15000 patients of the UNOS data base were analyzed, who were transplanted in the US from 2012 to 5/2016.
MELD-Na was calculated according to ths formula
MELD − Na − [0.025 × MELD × (140 − Na)] + 140 (na ranges from 125 to 140)
Delta MELD-Na was defined as MELD-Na at listing minus MELD-Na at transplantation: Delta MELD=MELD-Na (ON) − MELD-Na (TX)
Delta max was the highest MELD-Na deterioration between two observation time points.
Delta last was the alteration between forelast and last observation before transplantation.
Results: 66% of patients showed a stable MELD Na during waiting time for transplantation with a maximum increase of 2 points. In 8.7% of patients an increase of 3–5 points was observed. Further 5.7% of patients showed an increase of 6–10 points and 19.6% of patients showed an increase of more than 10 points. Only Delta MELD-Na deterioration by >10 points showed significant impact ($p = 0.002$) on posttransplant survival. Additionally MELD-Na TX und Delta Max ($p \leq 0.001$) were statistically significant risk factors.
Conclusion: A severe deterioration of MELD- Na during waiting time results in significantly poor post transplant survival in liver transplantation. Also temporary deterioration close to a potential transplant time point show similar risk. These acute deteriorating patients should only become transplants candidates again after recompensation and MELD-Na stabilization.

P19 RECONSTRUCTION OF HEPATIC ARTERY BRANCHES AND COMMON HEPATIC ARTERY BY THE USE OF VENA SAPHENA AUTOGRAFT AND ILIAC ARTERY ALLOGRAFT FOR LIVER TRANSPLANTATION

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Background: Harvest related grade 4 (Eurotransplant) injury of the donors' central hepatic artery are potentially life threatening to the recipient.
Methods: A liver from a 13-year-old female deceased donor was accepted for a 20-year-old male patient suffering from primary biliary cirrhosis. Backtable preparation prior to liver transplantation (LTx) revealed that both branches of the hepatic artery had been cut during organ retrieval. Microsurgical arterial reconstruction with running Prolene 8-0 suture was performed. Portal venous reperfusion was uneventful during LTx. However, the initially weak arterial flow (less than 50 mL/min measured by Doppler-Flowmeter) ceased within

10 minutes after arterial reperfusion. Thrombectomy with a size-2 fogarty catheter was not successful. Thus, complex arterial reconstruction was indicated. An autologous vena saphena graft was taken from the patient's left thigh and anastomosed (running suture, Prolene 7-0) with both arterial branches of the donor liver. Venous grafts were anastomosed with an iliac artery allograft in order to have enough length for a side-to-end aorto-iliac artery anastomosis (running suture, prolene 5-0).
Results: Arterial flow after reconstruction was normal with 200 mL/min and LTx could be completed without further challenge. The postoperative course was uneventful and the patient could be discharged at postoperative day 18.
Conclusion: High surgical expertise is a prerequisite for a low complication rate during organ retrieval. Early diagnosis of harvest related injury of the graft is crucial for effective intraoperative management. Autologous vena saphena graft and heterologous arterial graft are suitable for hepatic artery reconstruction.

P20 REDUCED SERUM CERULOPLASMIN CONCENTRATION IS COMMON IN PATIENTS WITH CIRRHOSIS AND A NAMELD INDEPENDENT PREDICTOR OF TRANSPLANTATION OR DEATH

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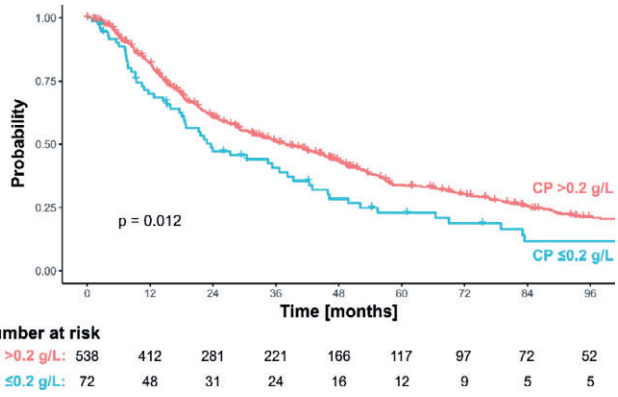
Background & Aims: Reduced concentrations of the plasma-ferroxidase ceruloplasmin (CP) are indicative of Wilson disease, but also commonly found in patients with NASH. The aim of the present study was to determine the prognostic relevance of CP in an unselected cohort of patients with cirrhosis.
Method: Patients referred for PNPLA3 to the University Hospital Innsbruck were included if the diagnosis cirrhosis was made.
Results: Reduced CP concentration of ≤0.2 g/L was present in 11.7% (72/613) of patients. The diagnosis Wilson disease had been made in 4 patients, only 3 of which had CP ≤0.2 g/L. The prevalence of low CP was 75% in Wilson disease patients and 23% in hemochromatosis patients followed by 16% in alcoholic cirrhosis and 13% in patients with NAFLD. Median NaMELD score was significantly higher in the patient group with CP <0.2 g/L (p=<0.001) and a significant negative correlation between CP and INR but not with albumin was found. Correlation-analysis further showed a significant association between CP and markers of iron metabolism/inflammation. Median time to transplantation or death as combined endpoint was also reduced in the group with low CP concentration (p = 0.012). CP but not PNPLA3 genotype was an independent predictor of the time to transplantation or death in a Cox-proportional-hazards model including age, NaMELD.
Conclusion: Hypoceruloplasminemia is common in patients with cirrhosis. CP is a NaMELD-independent predictor of survival indicating that ferroxidase-activity is implicated in the progression of cirrhosis.
Figure:



P21 THE INFLUENCE OF PREOPERATIVE ANEMIA ON ONE-YEAR MORTALITY AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Background: Anemia is a common condition in patients suffering from end-stage liver disease (1). In previous studies, preoperative anemia was associated with greater mortality in patients undergoing major surgery (2,3). The aim of this study was to investigate whether preoperative anemia influences one-year mortality in patients undergoing orthotopic liver transplantation (OLT).
Methods: This single-center retrospective study was performed at the Medical University of Vienna after local ethics committee approval. Patients undergoing their first OLT between 2004 and 2016 were included. Exclusion criteria were combined liver-kidney-transplantation and combined liver-lung-transplantation. Anemia was defined according to the classification of the WHO. Hemoglobin values were determined within 24 hours prior to surgery. To assess one-year mortality, a univariate cox regression model for death as event accounting for the combined factor of anemia (mild, moderate, and severe) was calculated.
Results: We included 607 patients with a mean age of 53 ± 8 years. Preoperatively, 24% (n = 146) of patients had no anemia, while 76% (n = 461) of patients suffered from anemia. Of the anemic patients, 28% (n = 172) had mild anemia, 42% (n = 252) had moderate anemia, and 6% (n = 37) suffered from severe anemia. Mean age of non-anemic patients was 55 ± 8 years while that of anemic patients was 53 ± 10 years (P = 0.01). During OLT, non-anemic patients required less intraoperative transfusion of red blood cell units than did anemic patients (2 ± 3 versus 4 ± 5 units, respectively, P < 0.001). One-year mortality after OLT did not differ between patients without preoperative anemia (21% mortality) and those suffering from preoperative anemia (21% mortality, hazard ratio 0.91, P = 0.66).
Conclusion: This retrospective study suggests that preoperative anemia is associated with increased intraoperative transfusion of red blood cell units but does not affect one-year mortality in patients with end-stage liver disease undergoing their first OLT.
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P22 PREDICTORS OF SUCCESSFUL DELISTING OF LTX PATIENTS

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Introduction: Due to chronic organ shortage, waiting list management becomes a challenge. This also includes patients who are rated as "too good" to be taken off the waiting list again. Although this is common practice in all TX-centers, there is little data as the basis of such a decision.
Methods: In a retrospective analysis of all patients delisted between 2006 and 2016 because of "too good", the decision was evaluated on the basis of the clinical outcome. The delisting was categorized as "correct" status if the patient was "alive without LTX", any other status (Relisting, LTX, Deceased) as "wrong". Patients with ACHF, pediatric-LTX, multi-organ transplantation and re-transplantations were excluded.
Results: 129 patients were included (f:m 41:88). Indications were ALCI n = 55 (42.6%), PHCB/C n = 30 (23.3%), HCCA n = 18 (14%), CYCI n = 7 (5.4%), CHOL n = 6 (4.7%), AUCI n = 5 (3.9%) and OTHE n = 8 (6.2%). In 53.5% the decision was "correct". While age had no effect, women were more likely to be falsely delisted than men (56.1% vs. 42.0% n.s.). In the indications, autoimmune and viral cirrhosis were critical with 20% and 33% correct decisions. Other indications showed better results with a 66–80% hit rate (p = 0.057). However, delta-MELD was significantly higher in the group of successfully delisted patients than in the negative outcome (−3.96 vs. −1.63 p = 0.002).
Conclusions: The analysis shows that age and gender have little impact for the delisting. The indication shows more influence, with "historical" data on the PHCC being questionably relevant. Highly significant influence, however, has the delta-MELD. This parameter appears best for selecting patients who are suitable for delisting.

P23 RECIPIENTS OF DCD LIVER GRAFTS TREATED WITH NRP DISPLAY LOWER POSTOPERATIVE MORBIDITY AND MORTALITY COMPARED TO STANDARD DCD LIVER GRAFT RECIPIENTS IN THE FIRST YEAR POST TRANSPLANT

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Background: Normothermic regional perfusion (NRP) was developed to attenuate the harmful effects of prolonged warm ischemia and subsequent cold storage caused during the process of donation after circulatory death (DCD) procurement. Herein we analyze the impact of NRP on postoperative morbidity and mortality following NRP-DCD liver transplantation (LT) compared to standard DCD LT during the first postoperative year.

Material and Methods: Medical records from patients transplanted with a standard DCD or NRP treated liver graft between January 2013 and June 2017 at the Edinburgh Transplant Centre were retrospectively analyzed.
Results: In the defined period 55 patients were transplanted with a standard DCD liver graft and 18 patients with a NRP treated DCD liver graft. There were no significant differences concerning recipient or donor characteristics between the two groups. When looking at early graft function, NRP liver graft recipients had significantly lower peak ALT levels during the first week compared to standard DCD recipients (503.28 IU/L vs. 1671.68 IU/L). While 4 patients (7.27%) in the standard DCD group suffered from PNF, none of the NRP recipients developed this complication. During the primary hospital stay standard DCD recipients had more Clavien-Dindo complications >grade III (43.64% vs. 27.78%), required more urgent re-transplantation (9.09% vs. 0.00%) and had higher mortality (Clavien-Dindo V in 3.64% vs. 0.00%) than patients in the NRP group. Regarding all complications within the first year post LT standard DCD recipients were readmitted more frequently and required a higher number of interventions such as liver biopsies (38.18% vs. 16.67%), MRCP (40.00% vs. 16.67%), CT-scans (60.00% vs. 33.33%), re-laparotomy (36.36% vs. 11.11%) and re-transplantation (16.36% vs. 0.00%) compared to NRP-DCD recipients.
Conclusion: NRP has a positive impact on postoperative morbidity and mortality of DCD liver graft recipients. NRP can aid in expansion of DCD utilization in light of the increasing shortage of donor organs.

P24 PREDICTORS OF SUCCESSFUL DELISTING OF LTX PATIENTS

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Introduction: Due to chronic organ shortage, waiting list management becomes a challenge. This also includes patients who are rated as "too good" to be taken off the waiting list again. Although this is common practice in all TX-centers, there is little data as the basis of such a decision.
Methods: In a retrospective analysis of all patients delisted between 2006 and 2016 because of "too good", the decision was evaluated on the basis of the clinical outcome. The delisting was categorized as "correct" status if the patient was "alive without LTX", any other status (Relisting, LTX, Deceased) as "wrong". Patients with ACHF, pediatric-LTX, multi-organ transplantation and re-transplantations were excluded.
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Conclusions: The analysis shows that age and gender have little impact for the delisting. The indication shows more influence, with "historical" data on the PHCC being questionably relevant. Highly significant influence, however, has the delta-MELD. This parameter appears best for selecting patients who are suitable for delisting.

P25 THE ROLE OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN LIVER TRANSPLANTATION

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Background: The clinical role of donor-specific anti-HLA antibodies (DSAs) in liver transplantation (LT) is not clearly established. We investigated the impact of the presence of DSAs on morbidity and mortality of LT recipients.
Materials and Methods: Between 2008 and 2015 649 LTs were performed at our institute. DSAs were determined by the Luminex® assay for all patients. Patients with positive DSA results at time of LT and in the post-transplant period were included. Transplant outcome was compared to a matched control group with no appearance of DSAs. The normalized mean fluorescence intensity (MFI) was used to quantify DSA levels and was correlated with clinical courses.
Results: 162 cases with class-I and/or class-II DSAs were identified and matched. One-year mortality was significantly higher in DSA positive patients compared to the control group (p = 0.037). There was no significant difference in the mortality after three, five and seven years. In both groups the leading cause of death was sepsis (38%). Within the DSA group, a MFI level over 8000 was associated with a significantly higher overall mortality, when compared to patients with low MFI levels (p = 0.042).
Conclusion: DSAs were associated with negative short-term survival after LT. This effect diminished in the long-term observation. Although high MFI-levels seem to correlate with the mortality, further investigations have to be made to detect risk factors for a negative outcome in patients with DSAs. Sepsis was identified as the leading cause of death. Therefore, future research needs to focus on the optimization of immunosuppressive regimes and treatment algorithms in this sensitive cohort, as LT recipients with positive findings of DSAs seem to be particularly prone to inferior outcome.

P26 HOSPITALIZATION AND LIFE SUPPORT BEFORE LIVER TRANSPLANTATION – EASILY AVAILABLE PREDICTORS FOR POST-TRANSPLANT PATIENT SURVIVAL

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Background: Currently liver allocation is based on urgency in many countries, mostly represented by the MELD score. To date, no applicable outcome predictors have been implemented for liver allocation. Aim of this study was to analyze the prognostic value of hospitalization and life support therapies prior transplantation (Tx).
Materials and Methods: All liver Tx from 2005 to 2016 were included. Life support was defined as dialysis accordingly to ET Liver Allocation System, mechanical ventilation and need of catecholamines.
Results: From 1244 liver transplant recipients, 264 underwent Tx coming from an intensive care unit (ICU), 178 from a regular ward and 802 from home. Patients coming from the ICU had a significant lower 3-months, 1-year and 3-year survival compared to patients coming from home (ICU vs. home; 76.9% vs. 94.4% and 65.9% vs. 87.5% and 64.4% vs. 82.4%; all p = 0.000). No differences were observed between patients from the ICU and a regular ward. Subgroup analysis revealed an ICU-stay longer than 6 days prior to Tx as a significant negative predictor of patient survival (p = 0.036). Dialysis prior to Tx was associated with an inferior patient outcome (p = 0.000). Life support therapy, ventilation or catecholamines alone did not influence survival. Patients with the triad of dialysis, ventilation and vasopressor therapy had the worst outcome with a 3-year patient survival of only 47.4% compared to 80% of patients without life support (p = 0.000).
Conclusion: Hospitalization status and life support before liver Tx are valuable predictors for patient survival after Tx and should be considered for the allocation process.

P27 GRAFTS FROM EXTENDED CRITERIA DONORS FOR LIVER TRANSPLANTATION

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Background: Organ shortage has driven transplant centers to extend their criteria for organ acceptance. In parallel donors have become increasingly older and multi-morbid. Extended donor criteria (EDC) have been defined; however, the impact of criteria on outcome after liver transplantation (LT) is under debate and has been assessed in our patients.
Patients and Methods: Between November 2016 and March 2018 49 patients (85.7% male) with a mean age of 57 + 11 years underwent LT in Graz for alcoholic liver cirrhosis (45%), hepatocellular carcinoma (41%), primary sclerosing cholangitis or autoimmune hepatitis (10%), HBV-associated liver cirrhosis (2%), and acute liver failure (2%). About 80% of grafts have shown EDC. To assess the impact of EDC on outcome after LT a retrospective analysis using both medocs and ENIS (Eurotransplant Network Information System) electronic data was performed.
Results: Primary dysfunction (PDF; 16.7%) and primary non-function (PNF; 6.1%) occurred in 98% of cases in EDC livers with a 90-day mortality of 3.6%. Further non-anastomotic biliary tract complications (18.4%) all occurred in ECD livers. Both AST/ALT levels elevated more than three times above normal values in organ donors together with a cold ischemic time of >10.5 hours was the strongest risk factor for biliary tract complications. The strongest risk factor for PDF and PNF was elevated AST/ALT and prolonged cold ischemic time as well together with a donor serum sodium of >165 mmol/L.
Conclusion: According to own results and existing literature, excellent survival results can be achieved with careful selection of ECD livers and appropriate recipient matching; however, there is an increased risks for complications (i.e. biliary) associated with the various types of EDC.

P28 DE NOVO USE OF EXTENDED RELEASED TACROLIMUS (ENVARSUS®) AFTER OLT – DOES THE COLONIC RESORPTION INFLUENCES THE OUTCOME?

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Introduction: Immunosuppression after OLT has reached a quite high standard with an excellent evidence level. However, there is still a lack of data for the de-novo use of Meltdose tacrolimus (Envarsus®, extended release) which has not only significant different pharmacodynamics but is also almost exclusively resorbed in the right colon compared to all other tacrolimus formulation that where uptaken in the small bowel.
Methods: In a single center pair-matched study we analysed 114 pts. early after OLT who either received Envarsus® (n = 57), prolonged released Tacrolimus (Advagraf®, n = 29) or immediate released Tacrolimus (n = 28) twice daily after induction therapy with ATG (1.5 mg/kgBW) together with steroids. Prolonged and immediate released Tac showed no difference in any outcome parameter so the controls were summed up for further analyses as enteric resorbtion group compared to colonic resorbtion study group. Study endpoints where therapy failure (death, graft loss, rejection), complication rates and Tac trough levels within the targeted range.
Results: As the patients were matched for Age, Sex and underlying disease there was difference is these parameters. One year patient and graft survival was 94% vs. 85% (n.s.)and 89% vs. 83% (n.S.) for the study group and the control group respectively. Rejection free survival was 95% vs. 88% at one year (n.s.) Bile duct insufficiency were found in 21% and vascular complications in 5% in both groups. Systemic infection episodes were diagnosed in 26% after OLT again equally in both group. Tacrolimus trough levels and seruem creatinine at 1 week, 1 month, 3 and 6 month as well as 12 month after OLT showed no significant difference at any time. No change of immunosuppression was induced by severe side effects.
Conclusion: Tacrolimus in its extended release formulation is a potent and easy to use immunosuppressant also denovo after OLT that is well tolerated by the patients. The outcome is not different to other tacrolimus formulations. So obviously the colonic resorption of Meltdose tacrolimus (Envarsus®, extended release) does neither impair the immunosuppressive potential nor does it have negative influence on complication rates. It might even be the tacrolimus formulation of first choice for patients with any kind of intestinal malfunction (small bowel syndrome, bariatric surgery etc.)

P29 EVALUATION OF THE CLINICAL UTILITY OF A LIVER FUNCTION TEST IN LIVER CIRRHOSIS: ASSESSMENT OF ACTUAL LIVER FUNCTION AND PROGNOSIS

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Background: Quantification of actual liver function is crucial in patients with chronic liver disease for monitoring of disease progression and individual prognosis. Non-invasive methods are required to reliably identify and quantify liver disease and its prognosis. The purpose of this study was to investigate the clinical utility of the liver maximum capacity (LiMAx) test in chronic liver disease (I) as a surrogate marker of liver function, (II) as a prognostic tool for the non-invasive evaluation of chronic liver disease and (III) as an estimate of short-term prognosis in such patients.
Materials and Methods: Adult patients with chronic liver disease were prospectively enrolled in a prospective observational trial between 2008 and 2013. In addition, we retrospectively evaluated data of cohort studies of patients undergoing partial hepatic resection or liver transplantation between 2004 and 2011 at our centre.
Results: Median LiMAx values differed significantly between healthy controls (n = 86) [412 (365–479) μg/kg/h] and cirrhotic patients (n = 269) [99 (57–160) μg/kg/h] ($p < 0.001$). LiMAx showed very good correlation with MELD ($rs = -0.686$; $p < 0.001$) and CPS ($rs = -0.707$; $p < 0.001$) and surrogate markers of hepatic functio n (PTT: $rs = 0.814$; $p < 0.001$; serum albumin: $rs = 0.761$; $p < 0.001$). 246 cases (182 hepatectomies and 64 liver transplantations) with surgical liver specimens were retrospectively analysed. LiMAx correlated significantly with histological classification systems (Ishak: $rs = -0.720$; $p < 0.001$; Desmet: $rs = -0.717$; $p < 0.001$). Median LiMAx was 357 (296–427) μg/kg/h in non-cirrhotic and 148 (92–213) μg/kg/h in cirrhotic patients ($p < 0.001$). AUROC for diagnosis of cirrhosis was 0.93. Using a cut-off of 240 μg/kg/h, cirrhotic patients were identified with a PPV of 84.5% and NPV of 94.3%. Of the 269 cirrhotic patients, twenty-seven died and twenty-seven received a liver transplant within 3 months of enrolment. The cox proportional-hazards model indicated that LiMAx (HR: 0.98; $p < 0.001$) and serum creatinine (HR: creatinine: 2.11; $p < 0.001$) were the significant parameters independently associated with the risk of liver-failure related death. Logistic regression analysis revealed LiMAx (RC: −1.344; $p < 0.001$) and serum creatinine (RC: −1.751; $p < 0.001$) to be independent predictors of mortality.
Conclusion: LiMAx appears to provide reliable non-invasive assessment of liver-cirrhosis and appears to be the independent predictor of short-term mortality risk in our cohort. This test allows a liver function-based graduation of disease severity and prognosis for the individual patient.

P30 PERIOPERATIVE CHEST DRAIN IN LIVER TRANSPLANTATION – AN UNCONVENTIONAL WAY TO REDUCE MORBIDITY

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Background: Liver transplant recipients are frequently affected by pleural effusions in the immediate postoperative phase with need of chest drain (CD) placement. The purpose of this study was to investigate the prevalence of drainage requiring pleural effusions after liver transplantation (LT) and post-interventional complications.
Materials and Methods: Adult LT recipients between 2009 and 2016 were analyzed retrospectively for pleural effusion formation and its therapy.
Results: Overall, 597 patients were included in the study. Of these, 361 (60.5%) had at least one CD placed within the first 10 days after LT. Patients with a Model for End-Stage Liver Disease (MELD) score >25 were affected more often (75.7% vs. 56.0%, $p < 0.001$). Typically, CDs were placed at the intensive care unit (ICU) (68.3%) or in the operating room (14.0% during LT, 11.0% during reoperations). In total, 97.0% of the patients received a CD on the right side, presumably caused by local irritations. Due to poor liver function pre-interventional optimization of coagulation was necessary in one third of interventions performed at the ICU. Out of 361 patients receiving an CD 14 (3.7%) suffered from post-interventional hemorrhage and 6 (1.4%) from pneumothorax requiring further medical treatment. Less complications were observed when performed in the operating room as compared to placement at ICU (1/116 (0.9%) vs. 20/316 (6.3%); $p = 0.019$).
Conclusion: Pleural effusion, more frequent in patients with higher MELD, is a common complication after LT requiring intervention in most cases. Routinely placed intraoperative CD may reduce complications, avoid unnecessary coagulation products and may prevent pneumonia.

P31 CURRENT EPIDEMIOLOGIC AND THERAPEUTIC TRENDS ON THE VIENNA LIVER TRANSPLANT WAITING LIST

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Background: Therapy for hepatitis C virus (HCV) infection, improved interventional/surgical management of HCC and optimized medical/endoscopic management of portal hypertension might have impacted on the need for liver transplantation. At the same time, obesity and the associated metabolic syndrome is increasingly prevalent.
Methods: Patients evaluated/listed for liver transplantation at the Medical University of Vienna between 04/2018 and 06/2018 were analyzed. We recorded the main etiologies and summarized the main indications for liver transplantation as following: (i) decompensated hepatic function, (ii) HCC, (iii) complications of portal hypertension (ascites/bleeding/HE), (iv) other. Finally we evaluate the proportion of patients receiving HCC downstaging.
Results: 99 patients were evaluated and/or listed for OLT in Vienna between 04/2018–06/2018. Regarding body weight categories: 17 (17.1%), 35 (35.4%) and 47 (47.5%%) are in the categories 60 kg, 70 kg, and 80 kg, respectively. Importantly, 47 (47.5%) of patients are overweight (BMI>25 kg/m^2), including 25 (25.3%) with adipositas (BMI>30 kg/m^2). The main etiologies were alcoholic liver disease (ALD: 37, 37.4%) followed by NASH/BASH (21, 21.2%) and viral hepatitis B/C (15, 15.2%%). However, non-NASH patients frequently presented with features of the metabolic syndrome. The most frequent main indications for liver transplantation was decompensated hepatic dysfunction in 47 (47.5%), followed by HCC in 27 (27.8%) and portal hypertension complications 21 (21.2%), and 4 (4.0%) other indications. Only 5/21 (23.8%) of patients with complications of portal hypertension had a TIPS implantation – and are undergoing regular paracentesis and/or repetitive band ligation. Recurrent episodes of severe hepatic encephalopathy and HRS-AKI represent major causes of unscheduled hospital admission. Among 27 patients listed because of HCC, 15 (55.6%) had received downstaging therapy and/or currently undergoing downstaging treatment.
Conclusions: NASH/BASH has become a major indication (21.2%) for liver transplantation at the Medical University of Vienna and metabolic liver disease additionally impacts on the progression of other etiologies. Most patients are listed due to decompensated liver function (47.5%%) and HCC (27.8%). While downstaging strategies have been largely adopted for HCC patients, the use of TIPS is underrepresented on the transplant waiting list.

P32 ANTICOAGULATION IN NON-MALIGNANT PORTAL VEIN THROMBOSIS IS SAFE AND IMPROVES HEPATIC FUNCTION

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Background: Non-malignant portal vein thrombosis (PVT) is common in patients with advanced liver disease. Anticoagulation (AC) increases the chances of recanalization and may improve liver function in patients with cirrhosis.
Methods: We retrospectively assessed the course of non-malignant PVT in patients receiving AC. Parameters related to hepatic injury (aspartate aminotransferase [AST]/alanine aminotransferase [ALT]), severity of disease (ascites) and synthesis function (albumin) as well as AC, rates of PVT regression/progression and AC-associated complications were documented.
Results: Among 122 patients with PVT, 51 patients with non-malignant PVT (27 incomplete, 24 complete) were included, 12 patients (25%) received long-term AC therapy (≥9 months) as compared to 36 patients without long-term AC. We observed a trend towards higher regression rates with long-term AC of 58% (vs. 28% without AC; p = 0.08) and lower progression rates of 25% (vs. 42% without AC; p = 0.15). In the subgroup of patients with decompensation prior to PVT diagnosis (n = 39), long-term AC (n = 10, 25.6%) resulted in a significantly higher rate of PVT regression/resolution (70% vs. 24%, p = 0.031). Interestingly, AST/ALT tended to decrease (−19%/−16%) and the proportion of patients with ascites became lower (−33%) with long-term AC (without AC: ±0%). Furthermore, there was a significant improvement in albumin levels (+9%/+3.6 g/dL) when compared to patients without long-term AC (−2%/−0.8 g/dL; p = 0.04). Additionally, 10 patients were treated with direct oral anticoagulants (DOACs) for splanchnic vein thrombosis. Importantly, there were no AC-associated bleeding events in patients with conventional AC and one bleeding event in patients with DOAC treatment (10%).
Conclusion: Our findings support anticoagulation in patients with non-malignant PVT, since AC seems safe and associated with superior PVT regression rates and might also decrease hepatic injury and improve liver synthesis.

LUNG

P33 SELECTIVE VENOUS CLAMPING DURING EX VIVO LUNG PERFUSION (EVLP) – INITIAL EXPERIENCE WITH 3 CASES

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Background: The shortage of suitable donor organs is still a major challenge in transplant surgery. Many donor lungs are rejected because of poor oxygenation capacity. Ex vivo lung perfusion (EVLP) provides the opportunity to reassess marginal donor lungs again and to identify possible causes for the poor organ function.
Methods: Indication for EVLP was set if donor lungs with macroscopical good organ quality had a poor global oxygenation capacity. By selective blood gas sampling during EVLP, the oxygenation capacity of each lobe could be assessed separately. If poor oxygenation was evident only in one lobe, it was removed from the circulation by selective venous clamping. Afterwards the global performance of the remaining lung was re-assessed. After EVLP, an anatomical resection of the clamped lobe and size-reduced lung transplantation was performed.
Results: From 07/2016 to 03/2018 three lung transplantation after selective venous clamping were performed. By clamping of the right (n = 1) or the left (n = 2) lower lobe, a delta pO2 > 300 mmHg could be reached. Thus, the organs could be accepted for transplantation. Subsequently, two trilobar and one single lung transplantation was performed. All recipients were female and the median age was 51 years (range 48–55). The underlying disease was lung fibrosis with ECMO bridging, exogenous allergic alveolitis and chronic obstructive pulmonary disease (each n = 1). All organs had an excellent organ function (Primary graft dysfunction score 0 after 72 h). The histological examination of the discarded lobes revealed mucopurulent bronchitis and bronchiolitis. During the postoperative course, one patient developed a sternal wound infection, otherwise no relevant infectious complications occurred. After a median follow-up of 18 months (range 3–22 Monate), all patients are alive.
Conclusion: By selective venous clamping during EVLP, not-transplantable donor lungs could be re-assessed and subsequently be accepted for size-reduced transplantation. In the future, this method might contribute to decrease the number of allocated but rejected donor lungs.

P34 OUTCOME AFTER LUNG TRANSPLANTATION USING MULTIPLE DECLINED MARGINAL DONOR LUNGS

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Background: Despite the implementation of extended donor criteria for lungs, acceptance rates of marginal organs still vary between transplant centers. One reason for this is insufficient data on parameters, which constitute a truly unacceptable donor lung. This leads to a substantial number of lungs being rejected and a significant reduction of the donor pool.
Methods: We analysed 749 patients who received double lung transplantation between January 2010 and June 2017 in our institution. A total of 124 patients were transplanted with donors previously rejected by two or more transplant centers. Of note, the reason for rejection was always concerns about the organ quality. A control group consisted of 625 patients who received lungs with none or only one previous rejection for quality reason. Short- and long-term outcomes between the two groups were compared.
Results: Pre- and intraoperative factors of both groups were comparable. Organ offers in Group I had been turned down between 2 and 12 times (median 3; IQR: 2–5). Main donor parameters did not show major statistical differences. However, there were significantly more offers with radiological infiltrations (p = 0.002), signs of lung contusion (p = 0.001) as well as abnormal findings in bronchoscopy (p < 0.001) in Group I. Despite this fact, rates of PGD 3 were comparable at all time points (t0: 13.2% vs. 18.1%, p = 0.318; t24: 2.5% vs. 2.2%, p = 0.402; t48: 1.7% vs. 3.2%, p = 0.765; t72: 0.8% vs. 2.7%, p = 0.432). Mean length of ventilation (119 vs. 118 hours, p = 0.958), ICU time (16 vs. 17 days, p = 0.647) und total length of stay (32 vs. 33 days, p = 0.729) were also similar. Survival (5 years: 72.6% vs. 75.8%, Log Rank: p = 0.970) as well as freedom from CLAD (5 years: 80.7% vs. 83.9%, Log Rank: p = 0.279) did not show significant difference.
Conclusion: A high percentage of donor lungs previously rejected by multiple other transplant centers for quality reasons can be safely utilized without a negative effect on short- and long-term outcome.

P35 INTER-OBSERVER VARIABILITY IN RADIOLOGICAL JUDGEMENT IMPAIRS GRADING OF PRIMARY GRAFT DYSFUNCTION AFTER LUNG TRANSPLANTATION

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Objectives: The current score for primary graft dysfunction (PGD) after lung transplantation relies heavily on chest radiographs and radiological judgement can make the difference between the lowest (PGD 0) and the highest (PGD 3) grade. This study aimed to evaluate inter-observer variability of the scoring of postoperative chest radiographs and its impact on PGD grades in a large single center cohort.
Methods: We retrospectively analyzed 497 lung transplantation recipients between 01/2010 and 07/2016. Three trained thoracic radiologists were asked to independently examine postoperative chest radiographs performed at *t0, t24, t48* and *t72* hours after arrival at ICU. Inter-observer variability was calculated using Cohen's kappa (κ) by pairwise comparison.
Results: A total of 1988 chest radiographs were evaluated. Consensus between all three radiologists was found in only 1087 cases (57.8%). At *t0* and *t24*, only a moderate agreement was found between the three radiologists (κ = .486 and κ = .473) and agreement was even worse at *t48* and *t72* (κ = .392 and κ = .412). At *t0*, PGD grading was 0 according to 2 radiologists in 20 cases (10.6%) but the diagnosis of the third would have led to a PGD 3. At *t24* this was true for 6 (1.2%), at *t48* for 4 (0.8%) and at *t72* for 4 (0.8%) cases, respectively.
Conclusions: The substantial inter-observer variability found in this retrospective analysis underlines the difficulty to adequately grade post-transplant organ function. Future revisions of the PGD grading should take this problem into consideration.

P36 LONG-TERM EXPERIENCE WITH ALEMTUZUMAB INDUCTION THERAPY: A SINGLE-CENTER ANALYSIS

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Background: Alemtuzumab is increasingly used as induction therapy in lung transplantation, however limited data on long-term results exist. We reviewed our experience and analyzed the impact of alemtuzumab on short- and long-term outcomes.
Methods: All patients, who received alemtuzumab, were included in this retrospective analysis. Following parameters were evaluated: survival, ACR, AMR, CLAD, malignancies and kidney function, DSA and infections incidence.
Results: Between 2008 and 2017 1051 lung transplantations were performed. 605 patients received alemtuzumab as induction therapy. Sixty patients (11.1%) developed kidney insufficiency. First infection was reported within the first 3 months in 308 patients (50%), within 3 to 12 months in 112 patients (18.5%). 10 patients died within the first year due to infections. Pseudomonas infection was observed in 69 patients (11.3%), CMV pneumonia in 18 (2.9%) and aspergillus infection in 92 (15.1%). Ten patients (1.6%) developed PTLD and 22 (3.6%) developed solid cancer. Cancer-related death was reported in 9 patients. De novo DSA were present in 41 patients (6.7%) in the first 90 days and in 46 (7.6%) patients thereafter. However, AMR was only diagnosed in 9 patients. At 1- and 5-years 97% and 96% patients were free from ACR. One and five-years freedom rates from CLAD were 97% and 79%. Overall survival rates at 1- and 5-years were 85% and 75%.
Conclusions: Our experience shows that alemtuzumab is an effective induction agent. It led to improved survival rates, fewer episodes of ACR and AMR and longer freedom from CLAD. Infection rate was higher, however, lethal outcome was only scarcely observed.

KIDNEY

P37 PASI-POET (PATIENT SAFETY IN PEDIATRIC ORGAN REPLACEMENT AND TRANSPLANTATION): FIRST RESULTS FROM THE EVALUATION OF PATIENT KNOWLEDGE IN THE CONTEXT OF A PILOT PROJECT

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Background: The informed patients and their relatives are key players in the management of their chronic diseases. Within our project PaSi-POeT, an evaluation of the patient's knowledge is carried out by means of a structured survey. Initial results reflect the level of knowledge of patients prior to the introduction of interventions for improving the health literacy.
Methods: For all patients who were discharged from May to June 2018 data on health literacy and socioeconomic data (knowledge of underlying disease and medication, cause of inpatient admission) were obtained (structured survey) and analyzed descriptively.
Results: Families (n = 31) with children (0–19.5 years, average age 6.5 years) who had a gastroenterologic (48%), nephrological (26%), rheumatological (7.5%) or other (18.5%) underlying disease were included in the study. More than 50% of the children were already patients at our division as infants. 80% of them (or the caretakers of these children) described themselves as children with a chronic disease. With an average of 4.8 different medications per patient (0–13 medications), less than one-third of the respondents were able to provide a complete and accurate answer concerning the medication (name, intake, medication category).
Conclusion: Children with chronic diseases respectively their caretakers have a significant lack of knowledge regarding their disease and treatment. This first results show the need as well as the potential of planned interventions for improvement of knowledge regarding diseases and treatments.

P38 STEROID PRETREATMENT OF ORGAN DONORS DOES NOT IMPACT ON EARLY REJECTION AND LONG-TERM KIDNEY ALLOGRAFT SURVIVAL

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Background: Systemic treatment of deceased donors with corticosteroids before organ harvesting reduced inflammation in the kidneys. However, the effect on biopsy confirmed acute rejection (BCAR) and longterm survival remains elusive.
Methods: In the current study 440 kidney recipients from 264 deceased donors were included. The donors were randomized to 1000 mg of methylprednisolone or placebo. We tested whether this intervention reduces the incidence of BCAR BANFF ≥1 within the first three months and improved the graft survival up to five years. A multivariable cox model with robust sandwich estimates was used to test the association for the treatment assignment with graft survival and find interactions with predicting variables. Covariables were selected by clincal expertise. The eGFR trajectories were assessed by a linear mixed model.
Results: BCAR was diagnosed in 23 (10%) patients of steroide group and 26 (12%) in the placebo group (p = 0.468). Five year graft survival was 84% and 82%, respectively (p = 0.941). The adjusted hazard ratio of functional graft survival was 0.9 (95% CI 0.57 to 1.42, p = 0.638). No effect modification was found for the treatment modality by predictors of graft survival. After five years the mean GFR was 47 mL/min/1.73 m^2 and 48 mL/min/1.73 m^2 (p = 0.756). The grand mean difference was 0.25 mL/min/1.73 m^2 (p = 0.887).
Conclusion: Despite suppression of inflammation in the graft early BCAR was not reduced through steroid treatment and did not show any association with functional graft survival.

P39 SUCCESSFUL EX VIVO EXPANSION OF BK-VIRUS-SPECIFIC T-CELLS FROM IMMUNOSUPPRESSED PATIENTS AFTER KIDNEY TRANSPLANTATION INDICATES POTENTIAL FOR ADOPTIVE T-CELL THERAPY

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Background: Patients after kidney transplantation are continuously immunosuppressed to avoid graft rejection. As a consequence, patients are highly susceptible to polyomavirus BK (BKV) infections, which cause BKV-associated nephropathy with graft failure in up to 30% of cases. Therapeutic options are limited and mainly based on reduction of immunosuppression, which, however, leads to acute graft failure in about 10% of patients. Recently, an association between reduced BK viral load and reconstitution of BKV-specific T-cells (BKV-T-cells) were seen in patients after kidney transplantation, emphasizing the importance of BKV-specific immunity. We aimed to verify whether BKV-T-cells derived from immunosuppressed transplanted patients with or without acute BKV viremia can be expanded ex vivo as a prerequisite for the adoptive transfer of BKV-T-cells.
Methods: For the ex vivo short-term expansion (STE), isolated mononuclear cells of 10 healthy donors (HD), 10 patients without (BKV-) and 10 patients with BK viral load (BKV+) were stimulated at day 0 and 6 with BKV-specific peptide pools and with interleukin 15 at day 9. After 12 days, cell products were characterized via IFN-□-ELISpot and intracellular staining of activation markers (such as IFN-□ and TNF-α) including detailed analyses of T-cell phenotypes via flow cytometry. Furthermore, cytolytic activity and potential alloreactivity of expanded BKV-T-cells against autologous and allogeneic target cells were assessed via flow cytometry.
Results: STE revealed highly specific BKV-T-cell spot forming colonies (SFC)/10^5 cells) from healthy donors (497 ± 31/10^5 cells), patients without (428 ± 19/10^5 cells) and with BK viral load (485 ± 21/10^5 cells) without significant differences between these groups. Generally in all groups, predominantly $CD4^+$ T-cells were expanded (HD: 58% ± 2.7 vs. BKV+: 60% ± 4.3 vs. BKV-: 65% ± 3.2) compared to $CD8^+$ T-cells (HD: 32% ± 2.5 vs. BKV+: 33% ± 3.4 vs. BKV-: 27% ± 3.1) among CD3. In all 3 groups, $CD8^+$ and $CD4^+$ T-cells showed an effector-memory (CD62L−/CD45RA-) and central-memory (CD62L+/CD45RA−) phenotype, known to induce fast and long-term immunity, respectively. Expanded $CD8^+$ as well as $CD4^+$ BKV-T-cells were "polyfunctional" as determined by secretion of different cytokines such as IFN-γ and TNF-α.

Conclusion: Successful ex vivo expansion and characterisation of patient-derived BKV-specific T-cells is a prerequisite for a potential follow-up study treating patients with BKV viremia.

P40 PREDICTING DONOR, RECIPIENT AND GRAFT SURVIVAL IN LIVING DONOR KIDNEY TRANSPLANTATION TO INFORM PRE-TRANSPLANT COUNSELING: A BEDSIDE RISK PREDICTION TOOL

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Background: The purpose of this study was to develop linked risk prediction models for living donor kidney transplantation candidate pairs at the time of counseling.
Methods: We used characteristics available from first single-organ transplantations performed at the Oslo University Hospital from 1854 donors between 1980 and 2007 with a median follow-up of 14.6 years, and from 837 recipients between 1995 and 2007 with a median follow-up of 13.1 years to derive multivariable Cox models to predict donor and recipient mortality, and graft loss. Deaths occurred in 195 donors and 255 recipients, and 162 grafts failed during the observation period until March 2015. Statistical analyses were done using R and SAS. Variables were selected using multivariable fractional polynomials optimizing Akaike's information criterion.
Results: Age, year of donation, smoking status, cholesterol and creatinine predicted donor mortality with a c-index of 0.821. Linear predictors from the donor mortality model served as parsimonious summary of donor prognosis and were considered among the candidate predictors for developing recipient models. Recipient age, recipient gender, calendar year of transplantation, pre-transplant dialysis vintage, primary renal disease, cerebrovascular disease, peripheral vascular disease, and HLA class II mismatch predicted recipient mortality with a c-index of 0.763. Recipient age, pre-transplant dialysis vintage, linear predictor of donor risk model, HLA class I and II mismatch, peripheral vascular disease, and heart disease predicted graft loss with a c-index of 0.682.
Conclusions: Our linked risk prediction models can be used to support informed decision making for living donor transplant candidate pairs using our webcalculator.

P41 GENOME-WIDE NON-HLA INCOMPATIBILITY BETWEEN DONOR AND RECIPIENT CONTRIBUTES TO KIDNEY ALLOGRAFT ATTRITION

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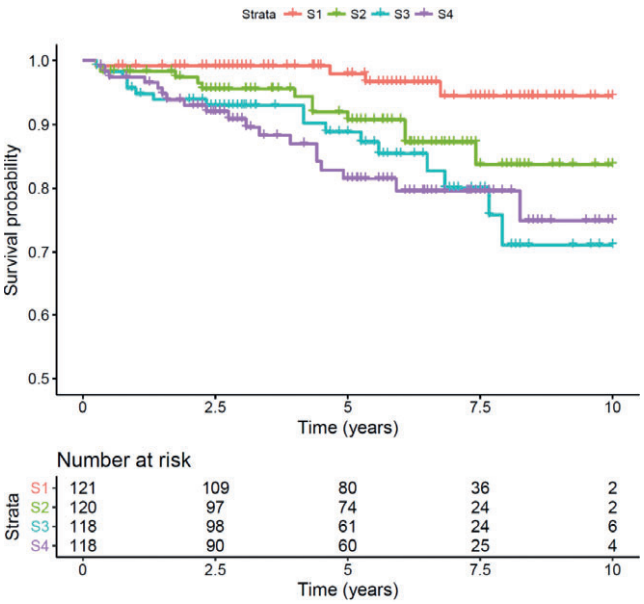
Background: The introduction of HLA matching of donors and recipients was a breakthrough in kidney transplantation but epidemiological data suggest also a fundamental role of non-HLA alloimmunity.
Methods: 477 deceased donor and first kidney transplant recipient pairs from a prospective multi-center transplant cohort study were successfully genotyped and genome-wide genetic mismatches in nsSNPs were calculated to identify incompatibilities in transmembrane and secreted proteins. Association of nsSNP mismatch and graft loss was estimated in a Cox proportional hazard model adjusting for HLA mismatch and clinical covariates. Customized peptide arrays were generated to screen for antibodies against genotype-derived mismatched epitopes.
Results: The median nsSNP mismatch in immune-accessible transmembrane and secreted proteins between donors and recipients was 1,892 with an interquartile range (IQR) of 86. The degree of nsSNP mismatch was independently associated with graft loss in a multivariable model adjusted for HLA eplet mismatch (HLA-A, B, C, DP, DQ, DR). Each increase by a unit of one IQR exhibited a HR of 1.68 (95% CI 1.17–2.41, p = 0.005). Five-year death censored graft survival was 98% in the quartile with the lowest mismatch, 91% in the second and 89% in the third quartile but only 82% in the highest quartile (p = 0.003, logrank test). (Figure). Customized peptide arrays verified a donor-specific alloimmune response to genetically predicted mismatched epitopes for selected transmembrane proteins.
Conclusion: Genetic mismatch of non-HLA haplotypes coding for transmembrane or secreted proteins is associated with an increased risk of functional graft loss independently of HLA incompatibility. Donor specific alloantibodies can be identified against genotype derived non-HLA epitopes.

Figure:



P42 RETROSPECTIVE EVALUATION OF CARDIOVASCULAR RISK STRATIFICATION PRIOR TO KIDNEY TRANSPLANTATION

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Background: Chronic kidney disease and kidney transplantation (KT) is associated with an increased risk for cardiovascular morbidity and mortality. In 2007 all Austrian KT centres accepted a consensus of comprehensive cardiovascular screening program prior to KT with the purpose to improve post-transplant cardiovascular outcome. The evaluation, how the consensus affected risk stratification and whether it has supported post-transplant cardiovascular success, is lacking.
Methods: In a single-centre retrospective study we included 504 patients, who underwent KT between 2003 and 2014 in the Medical University of Graz. Patients were divided in two 6-year cohorts: KTs before and after the consensus (n = 215 and n = 289 respectively). We included standard demographic and clinical characteristics, duration and type of renal replacement therapy, medication and typical cardiovascular co-morbidities in the analysis. Furthermore, we recorded the rate of coronary angiographies (CAG) and cardiac CTs prior to KT as well as post-transplant major adverse cardiac events (MACE) within 2 years following KT. Statistical significance of the differences between groups was tested using Mann-Whitney-U and chi-square tests respectively.
Results: Age, medication and the abundance of co-morbidities did not significantly differ from each other in the two cohorts. Significantly more cardiac CTs and CAGs were performed after the consensus. In less than 1/5 of all CAGs was a consecutive coronary intervention necessary. The occurrence of MACE did not show a significant difference in the two groups.
Conclusion: Cardiovascular risk stratification has become "more invasive" after the implementation of the 2007-consensus, yet an improvement of cardiovascular outcome is not reflected by our data.

P43 SUCCESSFUL SECOND KIDNEY TRANSPLANTATION IN A CHRONIC MYELOID LEUKEMIA PATIENT TREATED WITH IMATINIB

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Introduction: Active malignancy is considered an absolute contraindication for kidney transplantation (KTx). However, in the case of chronic myeloid leukemia (CML), tyrosine kinase inhibitor treatment with imatinib has converted CML to a chronic disease. Approximately two-thirds of imatinib-treated patients die of causes unrelated to CML. Moreover, immune surveillance may only marginally contribute to the natural course and therapeutic success of CML.
Patient: We describe the clinical course of a 56-year-old male patient with chronic kidney disease due to reflux nephropathy who had undergone first KTx 20 years ago and had again been on chronic hemodialysis for six years at CML diagnosis. First line therapy with 400 mg imatinib daily was well tolerated and induced molecular remission three months after initiation. After thorough and repeat counseling about the risks and benefits of continuing dialysis versus undergoing repeat KTx, he was wait-listed.
Results: One and a half years after CML diagnosis, a second KTx from a deceased donor was performed. Immunosuppressive regimen consisted of basiliximab, tacrolimus, mycofenolate mofetil, and corticosteroids. Currently, nine months post-transplant renal allograft function is stable (serum creatinine 1.3 mg/dL, CKD-EPI eGFR 60 mL/min/1.73 m^2) and CML remains in continuous molecular remission with imatinib. Imatinib therapy does not appear to affect immunosuppressive therapy as tacrolimus trough levels have so far been stable and within the target range.
Conclusion: This is the first report of a successful KTx in a CML patient under ongoing imatinib therapy. We conclude that imatinib-treated CML in remission should no longer be regarded as contraindication for KTx.

P44 RATES OF REJECTION AND INFECTIONS IN RENAL ALLOGRAFT ECD RECIPIENTS: COMPARISON OF TWO IMMUNOSUPPRESSIVE APPROACHES – A RETROSPECTIVE ANALYSIS

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Background: The use of kidneys from expanded criteria donors (ECD) addresses increasing donor shortage. Immunosuppression is largely center-specific with no clear data on optimal immunosuppressive strategy. However, reducing CNI levels in ECD has been suggested to achieve acceptable outcomes. This single-center study evaluated recipients in whom ATG induction was used while targeting lower CNI through levels and compared them to prior recipients who received standard immunosuppression (STD). Graft function, rates of major infections and biopsy-proven acute rejection (BPAR) were assessed.
Methods: ECD recipients were identified and parameters extracted from medical records. Major infections were defined as infections requiring hospitalization. The follow-up period was one year post transplantation.
Results: Twenty recipients (mean age 54 $\pm$ 11 years, n male/female 18/2, dialysis vintage 37 $\pm$ 21 months) were identified in the STD group and compared to twenty recipients (mean age 57 $\pm$ 10 years, n male/female 9/11, dialysis vintage months 44 $\pm$ 40) in the ATG group. There were no significant differences between donors in the STD (age 58 $\pm$ 12 years, last creatinine 0.8 $\pm$ 0.25 mg/dL, hypertension 35%, cerebrovascular cause of death [CVA] 80%) and the ATG (age 63 $\pm$ 7 years, last creatinine 0.76 $\pm$ 0.17 mg/dL, hypertension 40%, CVA 65%) group. FK506 through levels after three (10.5 $\pm$ 8.96 vs. 6.6 $\pm$ 3.23 ng/mL; $p < 0.05$) but not seven days (8.1 $\pm$ 2.21 vs. 7.86 $\pm$ 3.86 ng/mL; $p = 0.25$) were significantly higher in STD compared to ATG. There was no difference in occurrence of delayed graft function. A total of 6 BPAR occurred in 5 patients (4 (20%) in STD group, 2 (10%) in ATG group), one patient in the STD group experienced 2 BPAR. The risk of BPAR was 1,5 fold higher (RR 1,5 95% CI 0,28, 8,036) in the STD group vs. ATG group, but not statistically significant, possibly due to limited sample size. A total of 13 patients (6 (30%) in STD group, 7 (35%) in ATG group) required hospitalization during the follow-up. One patient (5%) of STD group suffered 2 major infections. During the first month after transplantation STD group showed no hospitalizations, while 1 ATG patient (5%) was hospitalized.
Conclusions: In this small retrospective study, limiting CNI exposure did not alter graft function, BPAR episodes or major infection.

P45 QUANTIFICATION OF TORQUE TENO VIRUS VIRAEMIA AS A PROSPECTIVE BIOMARKER FOR INFECTIOUS DISEASE IN KIDNEY ALLOGRAFT RECIPIENTS

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Introduction: Drug-induced immunosuppression following kidney transplantation is crucial to prevent allograft rejection, but increases risk for infectious disease. Tailoring of drug dosing to prevent rejection and infection at the same time is thus greatly desirable. The apathogenic and ubiquitous Torque Teno virus (TTV) reflects the immunocompetence of the host and might act as a potential candidate for immunologic monitoring.
Methods: To test the value of TTV as a predictive biomarker for infection, virus-levels were prospectively quantified in the peripheral blood of 169 consecutive renal allograft recipients in 2016 at the Medical University Vienna.
Results: Patients with infection showed higher levels of TTV compared to patients without infection (4.2×10^8 copies/mL, IQR 2.7×10^7–1.9×10^9 vs. 2.9×10^7, IQR 1.0×10^6–7.2×10^8; $p = 0.006$). Significant differences of TTV became evident almost 3 months before the infection (median 77 days, IQR 19–98). Each log level of TTV copies/mL increased the odds ratio for an infection by 23% (95% CI 1.04–1.45; $p = 0.014$). TTV levels above 3.1×10^9 copies/mL correspond to a sensitivity of 90% to predict infections. Logistic regression demonstrated an independent association between TTV levels and infection.
Discussion: TTV quantification predicts infection after kidney transplantation and might be a potential tool to tailor immunosuppressive drug therapy.
Keywords: Torque Teno Virus, Kidney Transplantation, Infection, Biomarker, Immunosuppression, Cytomegalovirus, Polyoma Virus Nephropathy

P46 FATIGUE AFTER LIVING KIDNEY DONATION

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Introduction: Numerous studies reveal living kidney donation – particularly considering prolonged graft survival as compared to postmortem organs – as the best therapy option for patients with terminal chronic kidney disease (CKD G5). In a previous study, the majority of donors did not experience any impairment in quality of life, but showed diminished performance and increased levels of fatigue. Therefore, we aimed to investigate various aspects of fatique appearance and chronic fatique syndrom (CFS) after living kidney donation.
Methods: Our study population included 27 living kidney donors in the period from 2015 until 2018 at the Medical University of Graz. Overall, these 27 individuals were tested with the semi-structured interview „SF-36 Fragebogen zum Gesundheitszustand" and „Gesundheit und Wohlbefinden nach der Lebendspende"-questionnaire from ÖBIG/GÖG. To identify the clinical diagnosis „Fatigue", we employed the Multidimensional Fatigue Inventory Test and the CFS-Interview for the Exploration of Chronic Fatigue Syndrome. Clinical diagnosis was made based on 5 symptom domains (neuroskeletal pain/fatigue, neurocognitive problems, inflammation, sleep disorder/fatigue and mood disorder).
Results: The donor population had a mean age of 52 (25–74) years and included 81% women and 19% men who underwent kidney donation at least 6 months ago. The majority of living kidney donors did not show health restriction and were not affected in performance status since donation. Resilience of 41% "slightly lower" and fatigue is "slightly lower" than before the donation of 36% more commonly reported by a donor (who was already 74 years old at the time of kidney donation) as "much more common."We identified fatigue in 10 participents, who nevertheless did not meet the criteria for chronic fatigue syndrome.
Conclusion: All kidney living donors participating in our study were satisfied with the decision to donate a kidney. Our explorative findings did not detect chronic fatigue in our study population, however found occurrence of fatigue. Study numbers need to be increased in order to allow a viable classification, this data indicate to focus pragmatically on severity and symptom patterns in order to reveal prognosis and success.

P47 COMPARISON OF PREOPERATIVE MAGNETIC RESONANCE ANGIOGRAPHY WITH INTRAOPERATIVE RENOVASCULAR ANATOMY IN LIFE KIDNEY DONORS

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Background: Life kidney donor evaluation includes imaging of the renal anatomy. Invasive digital subtraction angiography has been the gold standard while non-invasive magnetic resonance angiography (MRA) is available. Since reliability of findings after MRA remains unclear this study retrospectively compares preoperative MRA-findings with intraoperative reno-vascular anatomy of life kidney donors.
Methods: Reno-vascular anatomy of 22 living kidney donors were evaluated with gadolinium enhanced three-dimensional MRA from November 2016 to May 2018. Preoperative MRA results were compared to reno-vascular anatomy during mini-incision open donor nephrectomy and subsequent transplantation.
Results: MRA-findings have been confirmed intraoperatively in 72.7% of cases; however, in 22.7% of MRA the reno-vascular anatomy has not been shown appropriately. Fewer arteries have been confirmed during surgery in 4 cases while significant venous abnormalities have not been identified preoperatively. Uneventful transplantation without postoperative complications has been performed with immediate excellent graft function in all cases.
Conclusion: This analysis clearly shows that imaging with MRA does not adequately assess the reno-vascular anatomy in living kidney donors; however, number of arteries and veneous abnormalities do not correlate with complications in transplant centers with great expertise.

P48 TORQUE TENO VIRUS (TTV) IN RENAL TRANSPLANTED CHILDREN AND ADOLESCENT – A RETROSPECTIVE DATA ANALYSIS

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Background: The long-term function of transplanted organs is closely linked to a well-balanced state of immunosuppression (IS) and there is an urgent need for a useful assay to gauge the level of patients immunocompetence and to better guide the immunosuppressive therapy. In this respect, the monitoring of peripheral blood levels of a recently detected DNA-virus, called Torque Teno Virus (TTV), has been explored. Different studies have already shown that TTV-load seems to mirror the individual immunosuppressive state. Since data on TTV in renal transplanted children are scarce, the aim of this study was to investigate TTV and its association with various clinical and laboratory parameters in a cohort of kidney transplanted pediatric patients.
Methods: 45 kidney transplanted children at the University Hospital of Vienna, Austria, were included. TTV plasma load was measured monthly for a study period of one year and the relation of the virus DNA levels to different laboratory and clinical parameters were analyzed. Moreover, in a subgroup of six patients, for whom TTV-measurements were available before transplantation, the dynamics of the virus during the first three posttransplant months were assessed.
Results: TTV DNA was detectable in 94.5% of the tested samples. The assessment of TTV during the first three months, showed a significant increase of the TTV-load in all patients with the start of the immunosuppressive therapy. Moreover, a significant association with the post-transplant follow-up time (post-Tx-time), as well as with the type of immunosuppressive regime was found, with lower virus loads in patients after longer post-Tx-time and mTOR-inhibitor-based IS. Furthermore, a significant positive correlation with the dose of prednisolone and mycophenolate mofetil could be revealed. Regarding the relation of TTV plasma load and the occurrence of donor-specific antibodies (DSA) as well as the incidence of infectious complications and non-adherence, no significant association and correlation could be detected.
Conclusion: The data of this study further proves that TTV infection is widespread and closely related to the immune status. Concerning the use of TTV plasma load as a tool to guide the intensity of immunosuppression in renal transplanted children, further prospective and large-scale studies will be needed.

P49 SERUM AND URINARY BIOMARKERS FOR THE PREDICTION OF LATE ANTIBODY-MEDIATED KIDNEY TRANSPLANT REJECTION

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Study purpose: Antibody-mediated rejection (AMR) is a major cause of chronic allograft rejection and loss. Diagnosis is based on donor-specific antibody (DSA) detection and histological findings. Increased biomarker levels might reflect micro-inflammation and/or tissue damage in the biopsy of AMR patients. The purpose of this study was to identify serum and urinary proteins, which predict AMR in a DSA-positive patient collective derived from the screening phase of the BORTEJECT trial (ClinicalTrials.gov: NCT01873157).
Methods: Serum and urine samples of 86 stable kidney transplant recipients positive for donor-specific anti-HLA class I and/or class II antibodies (50 with biopsy-proven AMR, 36 AMR negative) from the BORTEJECT trial were tested for sE-Selectin, sVCAM-1, HGF, Granzyme B, CCL3, CCL4, CXCL9, CXCL10 and CXCL11. Laboratory experiments were carried out by single or multiplexed Human ProcartaPlex immunoassays (Thermo Fisher Scientific, Waltham, MA, USA) on the Luminex 200 platform.
Results: CXCL9, CXCL10 and HGF were elevated in serum samples of DSA+AMR+ compared to DSA+AMR- patients: CXCL9: median 412 vs. 276 pg/mL ($p = 0.002$), CXCL10 346 vs. 239 pg/mL ($p = 0.027$) and HGF 525 vs. 424 pg/mL ($p = 0.033$) respectively. ROC curve analysis of AMR revealed a superior predictive power of CXCL9 (AUC: 0.694) compared to CXCL10 (AUC: 0.64) and HGF (AUC: 0.635). All the other serum markers did not show statistically significant differences. Analysis of urine samples (normalized to creatinine) revealed improved results for CXCL9 and CXCL10 but not for HGF: CXCL9 median 43 vs. 13 pg/mg ($p < 0.001$), CXCL10 247 vs. 87 pg/mg ($p < 0.001$) and HGF 1369 vs. 1435 pg/mg; ROC analysis of AMR: 0.765 for CXCL9 and 0.756 for CXCL10.
Conclusion: We could identify CXCL9 as a promising biomarker in DSA+ kidney transplant recipients with a stable allograft in the prediction of late antibody-mediated rejection.

P50 SOLID ORGAN DONATION AFTER OUT OF HOSPITAL CARDIAC ARREST IN AVALANCHE VICTIMS – A RETROSPECTIVE ANALYSIS

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Background: Out of hospital cardiac arrest of avalanche victims often is associated with moderate to severe hypothermia. The most common cause of cardiac arrest in avalanche victims still remains asphyxia. If so, the development of a secondary hypoxic brain damage has to be expected (1–3). As hypothermia is proven to be cerebroprotective, a relatively liberal indication of prolonged extracorporeal life support systems (ECLS) is recommended (4,5). Nevertheless, the management of a cardiac arrest in avalanche victims is controversially discussed (6). As far as we know, there are no studies evaluating the incidence of solid organ donation in avalanche victims treated with ECLS compared to those patients without ECLS treatment.
Methods: The hypothermia database of Innsbruck Medical University Hospital was searched for patients with out of hospital cardiac arrest after avalanche burying. Data on circumstances of burial, body core temperature, survival, cause of death, duration of CPR, type of CPR (BLS, ALS, ECLS), ICU-Duration, pH-value, plasma potassium value, lactate value, Base Excess were recorded. In case of an organ donation the realised organ transplantations were recorded. Furthermore, type and number of donated organs and the primary transplantation outcome were recorded.
Results: At Innsbruck Medical University Hospital between 2001 and 2018, a total of 44 patients with hypothermic cardiac arrest after avalanche burial were treated. Only 11 patients (25%) survived until hospital discharge. All patient (n: 5; 100%) with ROSC after Basic Life Support (BLS) survived. Of those patients with ROSC after ALS (n:24) just 5 (20%) survived until hospital discharge. From the patients treated with ECLS (n: 15), just 1 survived (6%). 25 patients died because of a hypoxic brain edema (75% of non-survivors). 6 victims (18.2% of non-survivor group) became organ donors; 5 of those were from the ALS group (20%) and just 1 from the ECLS group (6%). In total 26 organs were donated; 11 kidneys, 5 livers, 4 hearts, 3 pancreases, 3 lungs. All organs were successfully transplanted.
Conclusions: Patient dying from brain death after cardiac arrest in avalanche burial can potentially donate organs. Our data give no indications that a liberal indication of ECLS after hypothermic cardiac arrest in avalanche victims leads

to an increase in survivors or an increase in organ donors. The probability of an organ donation after ROSC is higher in the ALS group (20%) than on the ECLS group (6%). Our data do not support a liberal indication of ECLS after cardiac arrest in avalanche victims in order to increase organ donors.

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P51 ROBOTER-ASSISTED KIDNEY DONATION

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Background: Minimal-invasive, laparoscopic kidney donation is offered in a number of centers performing living-donation kidney transplantation as standard procedure. Intraoperative problems occur more frequent in donors presenting with a body-mass-index >35 kg/m^2 and in those presenting with complex vascular situations (multiple arteries). Beside excellent results concerning intra- and perioperative complications a high acceptance in those patients is reported, ending up in an increasing number of obese donors as well as of donors with multiple arteries wishing to donate a kidney.

Methods: Since May 2017 we perform minimal-invasive nephrectomies with the help of the DaVinci robotic system in suited donors. Using a Pfannenstiel laparotomy, through which the graft is removed later on, two 8 mm tubes for instruments, one 10 mm tube for the camera and an Air-Seal-additional-port for the assistance (e.g. suction) the vessels and the ureter is identified and isolated, the kidney liberated from its fatty surrounding and vessels as well as the ureter are dissected using a 30 mm or 45 mm vascular stapler.

Results: Our first experiences, short-time results and a short video of the relevant steps of the surgical procedure are presented. In our series of 12 nephrectomies we had one conversion due to a venous bleeding from a lesion of the adrenal vein at its junction with the renal vein. There were no perioperative complications > Clavien-Dindo 1.

Conclusions: An international multi-center-analysis in 292 robotic nephrectomies shows similar results like in laparoscopic nephrectomies as well as our own data of the last 10 years. We suggest the use of this technique in other transplant-centers experienced in laparoscopic nephrectomies as well as robotic surgery. However, to avoid learning curves and guarantee outcome quality we recommend the application to a proctoring system. Furthermore, we feel ready for the next step, a fully robotic kidney transplantation, which is already performed in some highly experienced centers throughout europe.

P52 KIDNEY TRANSPLANTATION IN YOUNG CHILDREN: ASSOCIATION BETWEEN BODY WEIGHT AND OUTCOME – A REPORT FROM THE ESPN/ERA-EDTA REGISTRY

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Introduction: Kidney transplantation (Tx) in young children is challenging and requires multidisciplinary expertise. Many centres accept a minimum recipient body weight of 10 kg, but sound evidence-based knowledge is lacking. Therefore, we aimed to evaluate the current practice and outcomes of Tx in Europe.

Material and Methods: We included all patients who started RRT at an age <2.5 years and received a Tx between 2000 and 2015, and for whom body weight at Tx (<10 kg vs. >10 kg) was reported to the ESPN/ERA-EDTA Registry.

Results: 91 of 537 children received a Tx at a body weight <10 kg (median: 7.8 kg (IQR: 5.5–8.8)). The sex and primary renal disease distribution was similar in both groups. We found a significantly higher pre-emptive Tx rate for children < 10 kg (n = 15; 16.5%) compared with children >10 kg (n = 19; 4.3%) (p < 0.001). 13 patients died and 64 lost their graft during follow up. Mortality (<10 kg: 4.4%, >10 kg: 2%), graft loss (<10 kg: 18.9%, >10 kg: 13.5%) and particularly graft loss within the first 3 months (<10 kg: 41.2%, >10 kg: 46.7%) was similar in both groups. Body weight at transplantation was not associated with five-year-graft survival (aHR <10 kg vs. ≥ 10 kg: 0.92, 95% CI: 0.62–1.34).

Conclusions: We found no evidence for an increased risk of graft failure or mortality in Tx recipients <10 kg. We speculate that the decision for transplantation in young children is influenced by centre experience, local policies or complications of dialysis and primary renal disease.

P53 RENAL ARTERY ANASTOMOSIS TO A REMNANT RENAL GRAFT ARTERY FOR RE-TRANSPLANTATION WITH LIFE DONOR KIDNEY IN A PATIENT WITH III° CALCIFICATION OF THE AORTO-ILIAC AXIS

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Introduction: Arterial sclerosis is common in patients on dialysis for end-stage renal disease. Arterial anastomosis is challenging or not even feasible in these patients.

Case report: The 68 year old male patient in this report underwent simultaneous renal-pancreas transplantation 17 years ago. He received dialysis for kidney graft failure with the indication for re-transplantation for 7 months until a life donor was available. Unfortunately, the patient presented with III° arteriosclerosis of the aorto-iliac axis without possibility for an arterial anastomosis. However, preoperative ultrasound showed a patent renal artery of the 1st kidney graft. Thus, he underwent exploration before life organ retrieval. The arterial flow of his 1st kidney graft was confirmed intraoperatively before its removal maintaining the graft's artery in situ. The remnant of the renal graft's artery was assessed for anastomosis and an endarterectomy was performed to optimize its patency prior to completion of the end-to-end anastomosis with the artery of the new life donated graft.

Results: The final intraoperative arterial flow in the renal graft artery was great with 360 mL/min. An immediate postoperative standard duplex confirmed an excellent perfusion of the kidney graft with a good function without the need for further dialysis. The postoperative hospital stay was uneventful and the patient was discharged at day 16 after transplantation with serum creatinine levels of 1.35 mg/dL and an eGFR of 53.5 mL/min. Now, at four months after transplantation, the kidney graft function is stable (creatinine 1.35 mg/dL, eGFR 53.36 mL/min)

Discussion: In recipients with calcification of the aorto-iliac axis an exploration can be necessary to ensure the transplantability before nephrectomy of a life donor. Remnant renal vessels of a failed graft can be an option for anastomosis during re-transplantation. This case clearly shows the importance of an extensive preoperative evaluation.

P54 THE USE OF CHECKPOINT-INHIBITORS IN METASTATIC MELANOMA IN A COMBINED HEART AND KIDNEY TRANSPLANT RECIPIENT. A CASE REPORT

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Introduction: Immune-checkpoint inhibitors are promising agents in the treatment of metastatic melanoma. Transplant recipients are at increased risk of malignant diseases. While there is an urgent need for effective treatment of malignant melanoma in solid organ transplant recipients, only limited data are available for the use and safety of checkpoint-inhibitors in transplant patients.

Case Presentation: We describe a 77-year old, male patient, who had a stable transplant function over years after a combined heart (NT-pBNP 725 pg/mL) and kidney (eGFR 43 mL/min/1.73 m^2) transplantation. Initial immunosuppression consisted of tacrolimus, azathioprine and aprednisolon. Metastatic melanoma was diagnosed 12 years after heart- and 8 years after kidney-transplantation. Immunosuppression was switched to sirolimus, azathioprine and aprednisolon, because of the assumed antiproliferative effect of sirolimus. After detailed information about the potential risks and benefits he was initially treated with the anti-CTLA-4-antibody ipilimumab but suffered after a temporary partial response an acute biopsy-proven kidney-graft-rejection (BANFF Ib), as well as rapid progression of metastatic disease after 4 cycles of treatment. Cardiac graft function remained stable. Rejection-therapy with high-dose corticosteroids was partially successful and kidney-function was stabilized (eGFR 27 mL/min/1.73 m^2). Due to the urgent request of the patient for further therapy he received the PD1-inhibitor pembrolizumab. Acute, dialysis-dependent kidney injury as well as an acute decompensated heart failure (NT-pBNP >35000 pg/mL) followed 4 months after initiation of PD1-inhibitor treatment. A progress with a new solitaire brain metastasis was determined via CT~scan. Subsequently he developed a severe candida-sepsis and passed away despite extensive antimicrobial therapy.

Discussion: Limited data are available for the use of immune-checkpoint inhibitors in transplant patients. Based on the case presented here and review of the literature, we conclude that treatment with immune-checkpoint inhibitors can result in severe graft rejection and life-threatening complications in solid organ transplant recipients.

P55 LATE ANTIBODY-MEDIATED REJECTION (ABMR) AFTER KIDNEY TRANSPLANTATION – ROLE OF THE EGFR SLOPE WITHIN THE FIRST YEAR AFTER BIOPSY AS A SURROGATE ENDPOINT PREDICTING GRAFT FAILURE

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Background: There is currently no effective, evidence-proven treatment for late ABMR. Trial design in this particular context is a major challenge because the use of hard clinical endpoints would require exceedingly large sample sizes and immense follow-up. This retrospective study aimed to clarify the value of 1-year eGFR slope after diagnosis of late ABMR as a predictor of graft failure.
Methods: Study subjects were recruited upon screening of a large biopsy database (4615 eligible histomorphologic samples). Inclusion criteria were (i) transplantation between 2000 and 2013, and (ii) diagnosis of ABMR at >12 months post-transplantation (exclusion criteria: age <18 or >75 years; eGFR ≤25 mL/min/1.73 m^2). eGFR slopes were calculated using a mixed linear model with death-censored graft failure as the primary outcome variable.
Results: We identified 72 cases of late ABMR (median time to index biopsy: 34 months; range: 15–75). Seventeen (24%) biopsies showed active and 55 (76%) chronic active ABMR. Twenty-seven biopsies (38%) were C4d-positive. Median eGFR at the time of biopsy was 42 mL/min/1.73 m^2 (IQR: 39–45) and the median eGFR slope (first 12 months after ABMR diagnosis) was −4.4 mL/min/1.73 m^2. The decline of eGFR was tightly related to death-censored graft survival at 12, 24 and 36 months (eGFR slope above the median: 92, 92 and 88%; below the median: 72, 35 and 32%; $p < 0.001$).
Discussion: Our results reinforce the adverse impact of late ABMR on transplant outcomes. The early slope of eGFR was thereby found to be tightly related to graft survival, which may support its use as a surrogate endpoint for interventional trials.

P56 TECHNICAL CHALLENGES IN LIVING DONOR KIDNEY TRANSPLANTATION – DIAGNOSIS AND SOLUTIONS

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Introduction: Due to organ scarcity living kidney donation is becoming a major organ source for transplantation. Besides medical contraindications, anatomy of the kidneys may be a challenge for the surgeon. Multiple arteries and veins, short right renal vein and ureter duplex may be considered as a contraindication for living donation. We herein describe all recent living donor kidney transplantations (LDKTs) carried out at our institution with a focus on technical challenges, acceptance algorithm and side preference.
Material and Methods: Retrospective analysis of all LDKTs from October 2014-October 2017. Donor imaging has been carried out by multislice computed tomography with 3D reconstruction. Side selection has been based on an algorithm including 3MAG scintigraphy and anatomy. Endpoints were donor exclusion for anatomical reasons and vascular complications in the recipients.
Results: 100 LDKT were performed. No single donor has been excluded for anatomical reasons. Side preference was mainly based on lower 3MAG creatinine clearance (86%). In 14% the slightly better kidney was chosen due to anatomical reasons (multiple arteries n = 10, short renal vein n = 2, multiple renal veins n = 2). In 23 cases vessels were reconstructed backtable (multiple arteries n = 15, early branching n = 7, multiple veins n = 1) and in 2 cases a pole artery was anastomosed to the epigastric inferior artery. Ureter duplex was found unexpectedly in one case intraoperatively. One recipient underwent surgical revision due to kinking of the renal artery with favorable outcome. No kidney was lost due to surgical reasons.
Conclusion: Anatomical variations should not be a contraindication for LDKT. Microsurgical reconstruction and optimal choice of the side are crucial for favorable outcome.

P57 DE-NOVO GLOMERULONEPHRITIS IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION: A SINGLE CENTER REPORT

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Introduction: Retrospective center analysis of kidney and pancreas graft function, patient survival, major complications in 3 cases of biopsy proven de novo glomerulonephitis (GN) after simultaneous pancreas kidney transplantation (SPK).
Patients and Methods: The immunosuppression consisted initially of ATG, Tacrolimus, MMF, steroids and of Tacrolimus plus MMF at the occurrence of GN. The biopsy indication was an increase of serum creatinine and proteinuria (GN treatment: ACE-inhibitor/prednisolone).
Results: After a mean kidney survival of 118.6 months three patients (out of totally 435 SPK performed 1979–2007) developed a de novo GN at month 81/125/150 respectively, leading to graft loss after mean 17 months. One pancreas graft is functioning, one failed for thrombosis (month 1; retransplantation: chronic rejection, month 71), one for chronic rejection (month 149). The long-term immunosuppression at the time of occurrence of GN consisted of TAC (mean trough level 6.8 ng/mL) and MMF. The indication for biopsy was an increase of serum creatinine (mean 2.6 mg/dL) and proteinuria (mean 3660 mg/L). No critical infectious complication or malignancy occurred before the GN and no patient ever received an mTOR-inhibitor.
Discussion: De novo GN after SPK occurred at mean 118 months post-transplant (incidence of 0.007% correlating to the reported inferior limit of de novo GN after single-kidney transplantation) leading to graft lost after mean 17 months. An early biopsy in case of even mild proteinuria within normal serum creatinine is favorized. Further series reporting on this very rare complication would be useful to learn its detailed mechanisms.

P58 TANGENTIAL EXTRAPERITONEAL KIDNEY BIOPSY – TER: UPDATE

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Introduction: Safe and reliable biopsy techniques are mandatory for per protocol kidney transplant biopsies. A gold standard procedure as is percutaneous renal transplant biopsy (PRTB) in its field. We present the update of the clinical outcome of the Tangential Extraperitoneal Retrorenal (TER) approach, a specified technique for renal transplant biopsy that we have used over a period of 8 years.
Methods: Between 2011 and 2018, we performed 549 TER biopsies during 278 biopsy-events in 215 Patients. TER is an approximately horizontal lateral-to-medial approach performed by use of an automated biopsy device and 16-gauge needle size. Under real-time ultrasound guidance the utmost dorsal part of the kidney is adjusted and tangentially subjected to biopsy. By this technique, the peritoneal edge, the epigastric arteries, the renal pelvis and the anastomosis region are spared.
Results: No therapy requiring complications occurred (0%). There was one case of untreated gross haematuria and there were tree uncomplicated vasovagal reactions. Ultrasonography was performed routinely one day after the biopsy, we detected 31 small (under $3 \cdot 1$ cm) and 5 larger (over $3 \cdot 1$ cm) hematomas. Moreover 12 self-limiting AV fistulas appeared in Doppler ultrasound (2.1%). At a mean number of 1.8 ± 0.4 evaluated samples per biopsy-event, 93.8% of events were adequate to Banff '97 criteria. Educational biopsy events (37%) were equally safe and efficient as regular biopsies.
Conclusion: In comparison, the TER approach is the safest technique described for renal transplant biopsy, it provides good diagnostic efficacy and may be used in teaching hospitals.

P59 LIVING KIDNEY DONATION OF THE ELDERLY: CASE REPORT OF A 76-YEAR OLD KIDNEY DONOR

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Introduction: Living kidney donation is increasingly performed all over the world due to organ shortage. 1796 living kidney donations have been performed

in Austria until late 2017, were 37 (2.06%) were living donors between the age of 70 and 75 years and 10 (0.56%) were older than 75 years. Although 3.8–4.5% of all living donations in the US are currently older than 60 years of age, limited reports on donation safety in this age group is available.
Case report: In 05/2018, a living kidney donation from our so far oldest living kidney donor was performed. A 76 year-old female donor with mild hypertension (WHO I) and age-appropriate kidney function (Creatinin: 0.70–0.75 mg/dL; Cystatin C: 0.77–0.86 mg/L; eGFR CKD-EPI: 77.7–80.4 mL/min/1.73 m^2; eGFR combined Creatinin- und Cystatin C: 82.2–86.5 mL/min/1.73 m^2) donated for her 46-year old daughter. Measured GFR revealed a mGFR of 82.5 mL/min/1.73 m^2 and renal functional reserve of 85.5 mL/min/1.73 m^2. This increase after protein load can indirectly be considered as a sign of borderline normal vascular reactivity of the vas afferens. Estimation of the potential development of end stage renal disease using the „ESRD Risk Tool for Kidney Donor Candidates" (Johns Hopkins University, 2015) revealed a pre donation risc of 0.02% with a 0.27 times increase post donation.

Surgery was performed without complications, however the donor developed intermittent atrail fibrillation and temporarly reduced kidney function (AKI 3). After successful rhythm control, the donor was dismissed from hospital 8 days post surgery with a Creatinin of 1.13 mg/dL. Two weeks post donation, a Creatinin of 1.06 mg/dL and eGFR of 57.80 mL/min/1.73 m^2 was found and the donor was completely symptom-free. Recipient Creatinin was 1.14 mg/dL with a eGFR of 57.7 mL/min/1.73 m^2 at that time.
Conclusion: Living kidney donation in elderly (>75 years of age) requires special evaluation and consideration of risks, however should not firmly be rejected as a matter of principle.
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STEM CELL TRANSPLANTATION

P60 ECULIZUMAB FACILITATED STEM CELL ENGRAFTMENT AFTER PRIMARY REJECTION OF A HAPLOIDENTICAL BONE MARROW GRAFT FOR RELAPSED ACUTE MYELOID LEUKEMIA

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Introduction: Antibody mediated rejection (AMR) is an increasing problem in HLA mismatched, allogeneic stem cell transplantation (SCT). To reduce donor-specific HLA-antibodies (DSA), desensitization measures such as plasma exchange and rituximab are used. In case of insufficient antibody clearance, inhibition of the complement cascade is explored as salvage treatment in patients undergoing renal transplantation. However, this approach has never been reported in the setting of hematopoietic SCT.
Patient: We present a case of a 26-year old male patient with relapsed acute myeloid leukemia who suffered AMR of a haploidentical bone marrow graft. DSA were detected before transplantation and responded incompletely to desensitization with plasma exchange, rituximab and intravenous immunoglobulin (IVIG). Bone marrow aspiration on day +21 revealed primary graft rejection. The course was further complicated by multiple infections. Since leukemia was controlled at that time, the patient underwent another haploidentical transplantation with peripheral blood stem cells from the same sibling donor. This second haploidentical SCT was facilitated by eculizumab in order to prevent repeated AMR, since plasma exchange and IVIG again failed to sufficiently reduce DSA levels. On day +21 the patient engrafted successfully and is now alive 3 years after second haploidentical SCT.
Conclusion: Terminal complement inhibition with eculizumab has never been reported in the neutropenic pre-engraftment period of allogeneic SCT. Treatment with eculizumab may be feasible as salvage approach to prevent AMR when no alternative stem cell donor is available for urgent hematopoietic reconstitution in the setting of refractory leukemia or previous hematopoietic graft failure.

P61 HAPLOIDENTICAL BONE MARROW TRANSPLANTATION (BMT) IN OMENN SYNDROME UNDER INTENSIVE CARE TREATMENT AND ALTERNATIVE CONDITIONING

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Background: Omenn Syndrome is an autosomal-recessive disease (partial loss of RAG gene function), characterized by a severe combined immunodeficiency and opportunistic infections in the early childhood. The only curative option is an allogeneic stem cell transplantation. Without therapeutic steps, the disease shows a very unfavorable prognosis.
Methods: We here report on a patient with Omenn Syndrome who was in need of intensive care treatment with extracorporeal membrane oxygenation (ECMO) due to respiratory insufficiency, as a result of a fulminant adenovirus infection. After pulmonal improvement and clear reduction of the virus load, removal of the venoarterial ECMO was possible and we performed a haploidentical BMT from the mother at the age of six months. Conditioning was performed solely with ATG and post-Cyclophosphamide. Chemoconditioning is not possible at this critical health status and full graft function is not to be expected in T- cell depletion without chemotherapy. GVHD prophylaxis consisted of Mycopenolatmofetil and Tacrolimus.
Results: Full engraftment and mixed chimerism was seen already at day 15 after BMT. The generalized and typical rash disappeared completely and the adenovirus infection was under control. Even pulmonal function improved clearly despite long aplasia, so that extubation was finally possible. What followed was a transfer to our oncology ward in a good condition, 17 days after the transplantation procedure. Unfortunately, consequences like severe neurological symptoms with seizures and lacking eye contact followed. One month after the transplantation the patient died with a diagnosis of progressive encephalopathy with unclear genesis.
Discussion: Even under intensive care treatment and critical health status, an allogeneic BMT should be the intent in children with severe immunodeficiency syndromes. Haploidentical transplantation using post Cyclophosphamide could be a good option for these patients.

P62 RED BLOOD CELL DEPLETION OF BONE MARROW: COMPARISON OF TWO CELL SEPARATORS AND FIRST EXPERIENCE WITH SMALL VOLUME GRAFTS

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Red blood cell (RBC) depletion of bone marrow is advisable in blood group ABO major incompatible transplantation and – in the autologous setting – before cryopreservation of the bone marrow (BM) graft. We report about our experience with RBC depletion with two cell separators, the Cobe Spectra and the Spectra Optia, and we present first data of red blood cell depletion of small volume bone marrow grafts.

In the first period 11 BM grafts (8 allogeneic, 3 autologous) were RBC depleted with Cobe Spectra (CS; 1999–2009) and in the second period 11 BM grafts (8 allogeneic, 3 autologous) were RBC depleted with Spectra Optia (SO; 2013–2017) including 3 small volume (SV) grafts (all autologous) with the inevitable addition of third party packed red cells so that the RBC volume surpassed the limit of 125 mL for cell separation. Recovery rates for mononuclear cells (MNC), $CD34^+$ cells and the volume of the remaining RBC were calculated for the RBC depleted BM. Data are presented as median (range).

The total volume of the BM before manipulation and after RBC depletion was 1.43 L (0.77–2.35) and 0.13 L (0.11–0.30) for CS, 1.21 L (0.47–2.09) and 0.15 L (0.08–0.24) for OS, 0.49 L (0.47–0.68) and 0.11 L (0.10–0.11) for SV. The recovery of MNC in the RBC depleted graft was 91% (40–128) for CS, 83% (51–123) for SO and 80% (51–85) for SV. The recovery of $CD34^+$ cells was 113% (59–177) for CS, 96% (79–111) for SO and 88% (82–101) for SV. Remaining RBC volume was 7 mL (4–15) for CS, 7 mL (4–17) for SO and 5 mL (4–8) for SV, respectively.

The results show feasibility and safety of RBC depletion with both devices regarding cell recovery and residual RBC contamination. There were no significant differences between the two cell separators regarding MNC recovery and $CD34^+$ recovery, respectivly. The loss of $CD34^+$ cells in the three runs of small volume grafts were acceptable to achieve a transplantation dose in each case.