26th - 28th October 2023

Transplant International

Abstracts of the 32nd Annual Meeting of the German Transplantation Society, Jena, Germany, 26 – 28 October 2023

Introduction

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Die Jahrestagung der Deutschen Transplantationsgesellschaft findet jährlich im Herbst in Deutschland statt – in diesem Jahr am 26.-28. Oktober 2023 in Jena. Wir begrüßen etwa 600 TeilnehmerInnen aus allen Fachbereichen, die interdisziplinär im Gebiet der Transplantation zusammenarbeiten.

Neben den fachlichen Diskussionen zu den Themen u. a. Transplantation und Onkologie, Lebendspende, DCD, Erweiterung des Spenderorganpools, Maschinenperfusion ist der kollegiale Austausch enorm wichtig. Wir bieten 3 Plenarsitzungen, 21 wissenschaftliche Sitzungen und 7 Postervortragssitzungen an.

The annual conference of the German Transplantation Society takes place annually in autumn in Germany – this year on 26-28 October in Jena. We welcome about 600 participants from all interdisciplinary cooperation in the field of transplantation.

In addition to the technical discussions on topics including transplantation and oncology, living donation, DCD, expansion of the donor organ pool, machine perfusion, the collegial exchange is enormously important. We offer 3 plenary sessions, 21 scientific sessions and 7 poster sessions.

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12:15-12:30	Break			
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Oral Presentations

Quality of Structure / Process / Results

S01-05

Living In Harmony – Joining Hands And Data Without Exchanging Data Within The NephroCAGE Consortium

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Introduction

The NephroCAGE-consortium was initiated by two Canadian and one German transplant center to develop clinical prediction models (CPM) for kidney transplant failure. For CPM-training, data from multiple centers needs to be stored in one place. In the NephroCAGE-consortium we are avoiding that by harmonizing the data and training locally. Here we describe the harmonization and different demographics between Canada and Germany.

Methods

We performed a retrospective study using data of kidney transplant recipients from 1998-2019 in Center A, 2012-2019 in Center B and 2011-2020 in Center C. A data dictionary was defined to harmonize various data of recipient, donor and transplant features in a minimal and an extended dataset. Endstage renal disease, cause of death and type of donation were translated from German/French to English at first and then categorized further. Data harmonization in lab values was performed for units. Minimum and maximum limits for each lab value were created. Tests per patient in the first year were calculated using mean and median.

Results

At centers A-C 5558 patients were enrolled. In the minimal and extended dataset 46 and 88 features (minimal vs. extended dataset) were identified. Demographics and age distribution for each center are depicted in Table 1, respectively. The cold ischemia time was longer in Center B than in the other centers. Proteinuria detection using Protein creatinine ratio (PCR) was done 12.1$\pm$8.2 times in 59.6% patients (Center A) and 17$\pm$9.1 times in 96.4% patients (Center B) and using dipstick 36.4$\pm$8.9 times in all patients (Center C) within the first year. For legal reasons, donation after circulatory death is not performed in Germany.

Table 1

Parameter	Center A	Center B	Center C
Time period	1998-2020	2012-2019	2011-2019
N	4742	415	401
Recipient			
Male (%)	62.4	66.6	64.4
Age at transplantaiton (years)	51.3±14	55.5±12.4	57.9±12.8
Previous transplant (%)	12.9	0	0
Donor			
Age (years)	52.4±14.8	54.0±15.5	48.6±14.7
Male (%)	49.8	46.5	48.3
Transplant			
Cold ischemia time (hours)	8.6±5.9	13.7±7.9	8.8±5.3

Conclusion

There are differences between Canada and Germany regarding demographics, type of donation and aftercare processes. Along with harmonization, recognition of differences in clinical practice across participating centers is important to consider before training CPMs by FLI.

We like to thank Federal Ministry of Economy and Energy for funding this research.

Liver I – Limit Value Receivers

S02-04

Peak-MELD-Scores Of Patients Listed For Liver Transplantation (LT) Are Associated With Waitlist-Mortality And Impaired Access To LT

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Introduction
The Model of End Stage Liver Disease (MELD) Score is a widely accepted tool for liver allocation, but may be suboptimal for specific patients groups. Of note, infections are common drivers of decompensation and may therefore cause transient peaks of the MELD-score. Yet, in these scenarios, patients are frequently considered as not transplantable. In the present study, we aimed to analyse causes and consequences of peak-MELD-scores of patients listed for LT.

Methods
We performed a retrospective study on 172 patients registered for LT between 2020 and 2022 at the LMU Hospital. Patients without liver cirrhosis and with prior transplantation were excluded. The phenomenon "peak-MELD" was defined as follows: highest MELD within 6 months, increase by at least 5 points within 3 months, subsequent decrease by at least 5 points. Associations of the peak-MELD with mortality, non-transplantable status, infections and waiting time for organ offers were determined.

Results
A peak-MELD is a frequent finding in patients listed for LT, which affected 28% of all patients. Patients developing a peak-MELD were more likely to die prior to transplantation (Log-Rank Test; P=0.03) and there was a trend to a lower transplantation rate (30.8% vs. 64.2%; P=0.1). An explanation could be found in a high rate of infections during the development of a peak-MELD (66.7%) and a shorter time period on the waiting list in status "transplantable" following a peak-MELD (74.8% transplantable time vs. 87.3% in non-peak-MELD patients; P=0.02).

Conclusion
Patients with liver cirrhosis developing a transient peak-MELD-score have increased mortality and may have suboptimal access to LT.

S02-05

Circadian Rhythm Of Liver Transplant Donors May Affect Outcome After Liver Transplantation

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Introduction
The human circadian clock influences rhythmic physiology such as hormonal secretion, metabolism, detoxification and nutrient uptake. The central regulator of the circadian clock is located in the suprachiasmatic nucleus in the hypothalamus regulating local circadian clocks in peripheral tissues [1]. Impaired hepatic circadian clocks are associated with metabolic and inflammatory liver diseases [2]. In the preset study, we therefore aimed to

investigate associations of the circadian time of liver transplant donation with the outcome of patients after liver transplantation.

Methods
Clinical data were analyzed in 417 patients who had received a liver transplantation at the LMU University Hospital since 2014. Circadian times were defined as night (8 p.m. – 8 a.m.) or day time (8:01 a.m. – 7:59 p.m.). Associations between circadian time of donor liver harvesting and outcome of patients (survival, graft loss) was analyzed.

Results
Patients who received donor livers that were harvested during circadian day time showed a trend to a lower survival within 90 days compared to patients who received a liver that was harvested during circadian night time (86.3% vs. 90.9%, P=0.07). Of note, the circadian time of liver transplantation had no impact on the outcome of patients (P=0.9), making it unlikely that the performance of the medical teams during varying circadian times is responsible for the observed differences.

Conclusion
According to this preliminary analysis, the circadian clock state of the donor liver may affect survival after liver transplantation. Data on circadian clock gene expression will be presented.

References

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Heart I – Alternatives for Heart Transplantation

S03-04

Reducing The Immunogenicity Of The Heart By Genetic Engineering During Normothermic Ex-Vivo Heart Perfusion

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Introduction
Heart transplantation (HTx) is the only curative option to prolong lives of patients with end-stage heart failure. However, HTx is associated with major hurdles related to the limited number of organs available for transplantation, the risk of rejection due to genetic discrepancies and the immunosuppression (IS) burden. Previously, we showed that the silencing of swine leucocyte antigen (SLA) class I and class II expression in pulmonary grafts enabled graft survival after allogeneic lung transplantation even in the absence of IS. In this study, we aimed at evaluating the feasibility to decrease the immunogenicity of the heart by genetic engineering towards the reduction of SLA expression.

Methods
Lentiviral vectors encoding for shRNAs targeting β2-microglobulin sh(β2m) and class II transactivator (shCIITA) were delivered to the heart during normothermic

ex-vivo heart perfusion (EVHP). Hearts perfused with lentiviral vectors encoding for non-specific shRNA (shNS) or non-transduced (non-TD) hearts served as controls.

Results

Transduction efficiency was extremely high in all tpypes of heart tissue. Compared to shNS transduced hearts, silenced hearts showed up to 95% decreased SLA class I and up to 65% SLA class II-DQ expression, including the vascular endothelium as the major interface between donor and recipient. Histological analyses, perfusate troponin T (non-TD: 0.4±0.1 vs. TD: 0.2±0.1 ng/ml) and LDH levels (Abs A_{490}-A_{690}: non-TD: 0.961±0.1 vs. TD: 0.860±0.1) indicated no additional cell injury or tissue damage caused by lentiviral vector transduction in comparison to non-TD hearts after normothermic EVHP. Additionally, pro-inflammatory cytokine secretion signatures did not significantly differ between shβ2m/shCIITA and shNS transduced hearts.

Conclusion

This study clearly shows the potential of heart genetic engineering and its use in creating immunological graft invisibility. It is very likely that this technology will open up a completely new direction in overcoming organ rejection.

S03-05

Risk Stratification And Survival In Patients With Heart Failure Across The Spectrum Of LVEF: The Role Of Cardiopulmonary Exercise Testing In A Contemporary Cohort

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Introduction

The prognostic value of cardiopulmonary exercise testing (CPET) is established for risk stratification and as a selection criterion in candidates for heart transplant (HTx) in patients with heart failure (HF) and reduced ejection fraction (HFrEF). However, in patients with HFpEF and HFmrEF due to co-morbidities identifying patients with poor prognosis remains difficult.

Methods

We performed a single-center retrospective cohort study of ambulatory consecutive patients with HF (NYHA functional class I - III) irrespective of LVEF at the time of CPET. All patients underwent CPET evaluation with an upright bicycle between 2015–2017. The primary endpoint of all-cause mortality was assessed.

Results

For the primary analysis, 586 patients (mean age 61.7± 12.2 years, 28.2% female) were included. According to LVEF 282 or 48.1% of patients were classified as HFrEF, 82 or 14.0 % as HFmrEF and 222 or 37.9% as HFpEF. Patients were followed up for a median of 4.0 years (IQR: 3.4-4.9 years). Over this period, the primary endpoint occurred in 18.3% of patients. Patients in the HFpEF and HFmrEF group showed a higher mean peak oxygen uptake compared to HFrEF (pVO2; 17.3±5.8 and 16.9±5.3 vs 13.9±4.8 ml/min/kg, both p<0.001) and peak exercise power (Pmax; 106±43 and 112±48 vs. 89±36 Watt, p=0.02 and p<0.01). Peak oxygen pulse was also lowest in HFrEF (pO2/HR; 11.4±4.4 and 12.7±4.0 vs 10.3±3.9 ml/min/kg, p<0.001. Multivariable Cox-regression revealed pVO2 to be most predictive (HR +1 ml/kg/min: 0.88; CI:0.82-0.96, p:0.003) variable in the model while LVEF was not significant (p: 0.146). Using a predefined cut-off for pVO2 of 14 ml/min/kg Kaplan-Meier-Estimate showed a significant difference in survival for all groups of LVEF (Log Rank HFrEF: Chi^2: 15.8, p<0.0001, Log Rank HFmrEF: Chi^2: 10.05, p=0.02 and Log Rank HFpEF: Chi^2: 18.1, p<0.01).

Conclusion

As in HFrEF, CPET is a useful tool to stratify long-term risk in patients regardless of LVEF. Our findings also support the prognostic role of pVO2 as well as pO2/HR and Pmax in HF regardless of LVEF. Applying the cut-off of 14 ml/min/kg to the HFpEF and HFmrEF cohort revealed similar discriminatory value as in HFrEF.

Kidney I – Complication Management

S04-05

Intraoperative Fluorescence Lymphography To Prevent Lymphoceles In Kidney Transplantation

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Introduction
The occurrence of postoperative lymphoceles is one of the most frequent complications after kidney transplantation. In addition to asymptomatic courses, lymphoceles can cause serious complications that can result in graft loss. The incidence of symptomatic lymphoceles ranges from 0.03% and 26%. In our own cohort of living and postmortal kidney transplantation, the incidence of lymphoceles with the need of revision surgery was 7.2% in 140 consecutive kidney transplantations between 01/2019 and 12/2020.

Methods
Intraoperative fluorescence lymphography was performed in 16 consecutive living donor kidney transplants. 2ml of indocyanine green (ICG) (2.5mg/ml) was applied sonographically controlled subcutaneously into the lateral femoral trigonum next to the femoral artery. During renal transplantation, the integrity of the lymphatic vessels was documented at 3 different time points (before exposure of the iliac vessels, after exposure of the iliac vessels , after successful renal transplantation) using a fluorescence camera (Spy- Phi/Stryker). Postoperatively, weekly ultrasound checks were performed and an MRI of the transplanted kidney was performed 3 to 6 months after transplantation.

Results
16 consecutive Patients undergoing living donor kidney transplantation were analysed (w=7; m=9). The patients showed a median BMI of 27,4 ($\pm$ 3,7) kg/m^2, the time on dialysis was 329 $\pm$ 175 days. One patient underwent retransplantation and 6 patients were ABO incompatible transplantations. In all patients, the iliac lymphatic vessels could be identified and spared by ICG application. In the postoperative sonographic controls, no lymphocele was found in any of the analysed patients. The MRI scan of the pelvis performed after 3 months in the 8 patients that completed follow up already also showed no lymphocele. No adverse side effect due to the subcutaneous injection of ICG was observed in any of the patients.

Conclusion
In addition to valuable information on interindividual expression and location of the iliac lymphatic vessels, the intraoperative use of fluorescence lymphography has shown to be an effective and technically feasible method for sparing lymphatic structures during kidney transplantation.

S04-06

First Results Of The *Protect Renvarsus Study* (Protection Of Renal Function After Conversion Of Fast IR-TAC Meabolizers To Envarsus®)

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Introduction

In a proof-of-concept study we were able to show that fast immediate-release tacrolimus (IR-Tac) metabolizers showed an improved renal allograft function after conversion to prolonged-release tacrolimus (LCP-Tac), whereas slow Tac metabolizers had no benefit [1]. In this study, we hypothesize that this finding will be reproducible in a multicenter trial.

Methods

In a retrospective multicenter European trial, we aim to enroll 300 renal transplant (RTx) recipients who were switched from IR-Tac to LCP-Tac one month or later after RTx. In a 5-year follow-up, the development of renal function, diabetes mellitus, acute rejections and infections are observed. The C/D ratio at one month after RTx is used to define the two groups: fast IR-Tac metabolizers (<1 ng/mL*1/mg) and slow (≥1) [2,3].

Results

So far, a total of 99 patients have been included in this study. Initial findings have provided confirmation that fast metabolizers, who were switched to LCP-Tac early after RTx at a median time of 2.0 months (range: 1.0-253.1 months), exhibited improved renal function as measured by estimated glomerular filtration rate (eGFR). Conversely, slow metabolizers did not experience any recovery in eGFR even after switching to LCP-Tac at a median time of 13.2 months (range: 1.2-172.8 months) following RTx. The incidence of complications was infrequent and comparable in both groups.

Conclusion

The 5-year follow-up data will provide additional insights into the outcomes of patients after switch from IR-Tac to LCP-Tac.

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Lung Transplantation

S05-05

Oversizing Versus Undersizing Lung Allografts For Patients With Pulmonary Fibrosis: Results From A High-Volume Center

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Introduction

Lung transplantation is the only curative treatment for patients with end-stage pulmonary fibrosis. Due to the shortage of donor organs, the optimal donor-recipient size matching is nearly impossible, and most lung allografts are either oversized or undersized. It is still under debate whether over- or undersizing is better for the postoperative outcome. We therefore analysed our data using predicted total lung capacity (pTLC) to compare size-mismatches.

Methods

Records of patients aged between 5 and 80 years were retrospectively reviewed. Two groups were formed, one including patients with a donor-recipients pTLC-ratio (DRPR) of <1 (undersized group) and the other group with a donor-recipient pTLC-ratio of >1 (oversized group). Short- and long-term outcomes were evaluated using Chi-Square test, Mann-Whitney-U test and Kaplan-Meier analysis, respectively.

Results
Between January 2010 and May 2023, among the 1501 patients transplanted at our institution, 427 (28%) patients were included, 128 (9%) patients forming the oversized group (median DRPR: 1.04; interquartile range: 1.02-1.08) and 299 (20%) forming the undersized group (median DRPR: 0.92; interquartile range: 0.84-0.96). Patients from the oversized group had a longer ventilation time (p=0.004) and ICU stay (p=0.003). The incidence of PGD score 3 at 24 (p=0.031) and 48 (p=0.004) hours after transplantation was also significantly higher. No difference was seen in long term survival (p=0.70) and incidence of chronic lung allograft dysfunction (p=0.96).

Conclusion
Oversized lung allografts deteriorated early postoperative outcomes in patients with pulmonary fibrosis. Contrarily, long term outcomes were not affected.

Kideney II – Living Donation

S06-06

Social Characteristics And Early Experiences Of Living Kidney Donors In The German Living Donation Register SOLKID-GNR (Safety Of The Living Kidney Donor-German National Register)

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Introduction
The prospective Register SOLKID-GNR was established to provide clinical and psychosocial outcome data on living kidney donors (LKD) in Germany. We investigated social parameters as well as early experiences in the evaluation process of becoming a LKD.

Methods
Social baseline data were collected prior to and outcome data 12 months after Living Donation (LD).

Results
Most of the LKD were female (63%; female 54.5 ± 9.9 years; male 53.7 ± 10.5 years). 97.2% of the enrolled LKD were caucasian (7 asian, 2 african, 1 hispanic), 89.5% were born in Germany. 11% of donors were excluded due to insufficient German language knowledge.

Recipients were in 44.8% spouses, 34% children, 13.7% siblings, 1 mother and 7.5% others.

Concerning education, LKDs´ highest school-leaving qualification was 33.8% senior high school (Hochschulreife), 40.3% high school (Realschule), 22.5% high school (Hauptschule), and 1% no final school exam. Highest vocational qualification was 23.3% university degree, 9.2% technicians´ degree, 60.4% vocational qualification, and 7.2% no qualification. 53.1% LKDs reported to be full-time employed, 20.7% regular part-time (min.15 hrs/w), 4.93% irregular part time (max. 15 hrs/w), and 21.3% not being employed.

Duration of complete pre-donation medical diagnostics was >12 months 31.5%, 6-12 months 39.1%, 3-6 months 21.5%, and <3 months in 8% of LDs. 45.5% of LKD complained about too long, 0.32% about too short preparation time, and 54.2% were satisfied with the length of preparation.

Pre-donation, 96.8% LKD reported to be very well or well informed, whereas 0.95% reported to be badly or very badly informed. One year after LD, 93.7% LKD reported about very good or good information and 3.34% about bad or very bad

information.One year after LD 86.94% LKD would definitely donate again, 8.21% were rather willing, 2.6% were undecided and 2.2% were rather not willing to donate again.

Conclusion

Nearly two-third of the LKD were female, and more than 90% donated to a near family member. More than half of the LKD were full-time employed at the time of donation. Most of the LKD were satisfied about the information process pre-donation, and would be willing to donate again.

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Immunology

S07-08

Significance Of Complement-Dependent Cytotoxicity (CDC) Crossmatches For The Prevention Of Unsuitable Organ Offers In Eurotransplant Kidney And Pancreas Transplantation Programmes

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Introduction

Since April 24th, the classic complement-dependent cytotoxicity (CDC) allocation crossmatch for kidney and pancreas transplantation is omitted. After a virtual crossmatch (comparison of donor HLA typing with recipient unacceptable antigens), organs are shipped to the recipient centre, where the transplant crossmatch is still performed by CDC. The number of unsuitable organ offers recognized by a positive CDC crossmatch but not by the virtual crossmatch is unknown.

Methods

Since June 2018, Eurotransplant (ET) informs the recipient HLA laboratories about all positive donor center CDC crossmatches. All such reports for two transplant centres until April 2023 were evaluated.

Results

13 positive CDC crossmatches were reported (about 0.8% of crossmatches): 7 were from patients in the ET senior or pancreas programme, for whom no virtual crossmatch had been performed prior to the CDC crossmatch. 1 was from a patient with strong antibodies against one allele of the donor's antigen DR4 (DRB1*04:02, 20.000 MFI), which could not be entered as unacceptable antigen in 2019. 2 positive CDC crossmatches were from a highly immunized patient with several donorspecific antibodies (DSA, cumulative MFI 12.000 and 27.000, respectively), for whom only C1q-positive antibodies were assigned as unacceptable. A further positive crossmatch was from a patient with a weak DSA (MFI 3000), for whom only strong antibodies had been entered as unacceptable. 2 crossmatches were for donors without DSA, but with known DTT-sensitive positive reactions in CDC (PRA without DTT 4-10%, with DTT 0-4%).

Conclusion

Almost all positive CDC crossmatches reported during the last five years were due to imperfect performance of virtual crossmatches before January 2023 or intended incomplete assignment of HLA antibodies as unacceptable antigens. Two positive CDC crossmatches were presumably caused

by DTT-sensitive Non-HLA-antibodies, which are generally considered as clinically irrelevant.

If all HLA antibodies are entered as unacceptable antigens, a negative virtual crossmatch reliably predicts a negative CDC crossmatch. Omission of the CDC crossmatch could be feasible for large patient groups.

S07-09

From HLA Antigens To Alleles And Back: Serotypes, Matching Determinants, EpiArt

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Introduction

HLA typing went through different evolutionary phases, starting with serological typing to molecular means, edging into the next and third generation sequencing, which allows typing for 11 loci in 4-5 hrs, deemed suitable for postmortem solid organ typing. To use the results for allocation purposes within Eurotransplant a transcription to matching determinants is needed. The role of HLA-specific antibodies gained a central role in transplantation as so-called unacceptables used for virtual crossmatching. Antibodies bind to designated epitopes, which are shared between HLA alleles in an intralocus and interlocus manner. We aimed at visualizing the HLA epitope distribution among alleles and thus help validate HLA antibody reaction patterns, define unacceptables and facilitate the virtual crossmatch.

Methods

In this collaborative study, we used the common HLA-A alleles found in the German population (hla.alleles.org) and their amino acid sequence information (IMGT/HLA) to analyze/visualize the epitope distribution among them. The alleles form groups, which are similar but more detailed to the antigens reported earlier. The alleles were translated into antibody confirmed epitopes using the epregistry.com.br.

Results

Here, we concentrate on the HLA class I alleles. The 295 included in the study expressed several antibody confirmed epitopes. The frequency of the epitopes ranged from 2-130. Several of the alleles, e.g., HLA-A*01:01, A*01:02, and A*01:03, although differing in DNA sequence and name are in terms of epitopes identical. The most frequent HLA-A allele-group, HLA-A*02, is represented in the study by 20 alleles. 13/20 are identical in terms of epitopes. The remaining have minute differences to that group. Within HLA class I the most alleles within a group shared the epitopes which were different to the other alleles and allele groups.

Conclusion

These results, allow on one side the visualization of the HLA-A polymorphism (EpiArt), while on the other side their use as matching determinants (equally valued) simplifies the allocation procedure and facilitate the virtual crossmatch. Strictly spoken, they explain the probably temporary use of matching determinants in the allocation procedure.

Liver II – Achilles Heel – Bile Duct After Transplantation

S08-04

Studying Ischemia/ Reperfusion Injury In Liver Transplantationusing Extrahepatic Cholangiocyte Organoids

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Introduction
Biliary complications are still a major cause for morbidity and mortality after liver transplantation. Ischemia/ reperfusions injury (IRI) leads to disruption of the biliary epithelium. Yet little is known about the underlying molecular mechanism. We introduce a novel model to study the effect of IRI on human cholangiocytes using extrahepatic cholangiocyte organoids (ECOs).

Methods
Extrahepatic bile duct tissue was collected during liver transplantation at static cold storage and after reperfusion (n=15). Gallbladder tissue was used as control (n=5). ECOs (n=9) were cultured from extrahepatic biliary tissue. IRI was induced in ECOs by introducing cells to a hypoxic chamber for 48 hours and subsequently to 24 hours of reoxygenation. Multiplex immunofluorescence, in-situ hybridization and qRT-PCR were performed to study markers for hypoxia as well as programmed cell death.

Results
After reperfusion an activation of programmed cell death was observed in the biopsies obtained during liver transplantation (p=0.0002). Cultured ECOs self-organized into circular structures recreating a tubular structure similar to that found in the bile duct. Immunofluorescence and qRT-PCR verified cholangiocyte phenotype of the ECOs. After hypoxia ECOs showed increased expression of ACSL4 (p<0.0001) and VEGF-A (p<0.0001). HIF1-a expression was increased after reoxygenation (p=0.0003). Expression patterns were similar to those found in the bile duct biopsies obtained during liver transplantation.

Conclusion
ECOs are in-vitro cellular systems that self-organize through mechanisms like those found in-vivo. They recapitulate the structure and exhibit similar patterns of ACSL4, VEGF-A and HIF1-a expression as extrahepatic bile duct during liver transplantation and thus provide a suitable model to study IRI in choanocytes after liver transplantation.

Heart II – Current Developments in Heart Transplantation

S09-05

Echocardiographic Speckle-Tracking Derived Parameters Of Right Atrial But Not Left Atrial Strain Are Associated With Cellular Rejection In Patients After Heart Transplantation

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Introduction
Speckle-tracking derived strain echocardiography (SE) has developed into a suitable screening-tool for subclinical acute cellular rejection (ACR) in patients after heart transplantation (HTx). While several studies report an association between impaired ventricular strain and ACR, data on the impact of atrial strain are lacking. We aimed to compare the significance of ventricular and atrial strain with respect to an associated ACR.

Methods
Patients who received endomyocardial biopsy (EMB) within 1 year after HTx were eligible for this retrospective analysis. Patients' records were screened for EMB results and corresponding echocardiograms, preferably performed at the same day. SE analyses were performed offline using a dedicated software (AutoSTRAIN, TomTec): left ventricular (LV) global longitudinal strain, right ventricular free wall strain (RVFWS), left and right atrial reservoir strain (LASr, RASr), conduit, and contraction strain (LASct, RASct). The relationship between SE and ACR was assessed by groupwise comparisons and regression analysis.

Results
EMB results of 52 patients (median age 53 years (IQR 47-62), 63 % male) after a median of 181 days (IQR 105-297) post HTx were identified. Mild ACR was present in 19 patients, and ≥ moderate ACR in 6 patients. Mean LVEF was 60 % (± 6), mean TAPSE was 15 mm (± 3). On groupwise comparisons, any ACR (mild to severe) was associated with impaired RVFWS (p=0.015) and with impaired RASct (p=0.044). On logistic regression analysis, ACR ≥ moderate was associated only with RA strain (RASct: OR 1.23, 95%CI 1.04-1.54; p=0.034; AUROC 0.80; RASr: OR 0.91, 95%CI 0.81-0.99; p=0.043; AUROC 0.80). RASct higher than -14.3 % (indicating worse contractility) had a sensitivity of 100% and a specificity of 54 % for the diagnosis of ≥ moderate ACR. Interestingly, none of these associations was seen for LV or LA strain values.

Conclusion
Our comprehensive semi-automated strain analysis confirmed the association between reduced RVFWS and ACR, but could further identify robust associations between RAS and ACR. However, SE of the left heart did not show associations with ACR. RA strain analysis may be a promising method for the detection of subclinical ACR after HTx.

Ethics

S10-04

Potential Organ Donors In Hospitals Without Neurosurgery – An Underutilized Donor Source ?

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Introduction
Identification of potential brain dead donors (DBD) requires expertise as well as routine. Donor hospitals in Germany are designated as university hospitals (A), hospitals with neurosurgery (B) and all other hospitals with ICU facilities but without neurosurgery (C). We investigated whether DBD donor profiles differed between these categories of donor hospitals.

Methods
The database of German National Organ Procurement Organization (OPO, Deutsche Stiftung Organtransplantation - DSO) is prospectively maintained. 21.250 datasets of potential DBD donors from 2006 - 2013 were analyzed retrospectively, data were pseudonomized. Demographic donor parameters including age, sex, cause of death, decision for or against organ donation , realised donoations, time interval from admission to hospital and duration of organ retrieval procdures were analyzed with regard to different categories of donor hospitals.

Results
Crude numbers showed the highest number potential donors (PD) in B (8.323), followed by C (6.523) and A (6.404). C had a higher number of older PD (>65 yrs): 40% vs. 30% (B), vs. 33% (A). Secondary brain damage was observed more often in C (2431) vs. A (966) and B (813). The most frequent diagnosis leading to DBD in C was hypoxia (2495), compared to intracranial bleedind (ICB) in A (1714) and subarachnoid bleed (SAB) in B (2501). Discontinuation of the organ procurement process due to medical reasons before interviewing next of kin occured most often in C (1860) followed by B (1232) and A (1141). Realized organ donations were 3447 (A), 4208 (B), and 4071 (C). Duration of organ retrieval did not differ substantially between hospitals (median duration: A – 2.8 hrs, B – 2.8 hrs, C – 2.6 hrs).

Conclusion
Potential organ donors in C hospital were older with a larger proportion of secondary brain dmage, most frequently due to hypoxia. Medical reasons most often led to discontinatuion of the organ donations process, even before next of kin could be interviewed with regard to consent. Hospitals without neurosurgery may be an underutilized source of DBD donors.

This abstract is based upon data from the doctoral thesis of Sigrid Blehle. The help of all transplant coordinators of the DSO as well as local staff at donor hospitals with data collection is gratefully acknowleged.

S10-05

Extracorporeal Life Support (ECLS) Facilitated Organ Donation: A Transplant Centre's Experience

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Introduction

Hypoxic-ischaemic encephalopathy (HIE) following cardiac arrest (CA) is a significant cause of brain death (BD) [1, 2]. Extracorporal life support system (ECLS) may be indicated in cases where conventional measures fail after cardiac arrest [3]. Current guidelines may lead to an increase in ECLS use during cardiopulmonary resuscitation (CPR), hence an expected rise in the number of ECLS supported organ donors.

Methods

In a retrospective analysis of data from our center between January 2021 and December 2022, a total of 25 successful organ donations were identified, of whitch two organ donations were carried out under ECLS.

Results

Organ Donation 1: Middle age, CA due to cardiogenic shock following acute myocardial infarction. ECLS implantated one hour later during CPR. Initial signs of brain herniation observed five hours post-implantation, with brain death diagnosed two days post-cardiac arrest. Organ Donation 2: Middle age, CA due to malignant arrhythmias and cardiogenic shock following self poisoning. ECLS was implanted one hour later during CPR. Brain herniation signs observed twelve hours post-implantation, and brain death was diagnosed three days post-CA. In both cases, liver and kidneys were explanted. The organ quality was assessed as good at the time of explantation. However, the liver in the second case was considered inadequate for transplantation due to microvesicular steatosis on histologic analysis. The remaining five organs were successfully transplanted with a good one-year function. Only one transplanted kidney showed a transient moderate dysfunction due to an infection at the time of data collection.

Conclusion

ECLS is increasingly used during CPR, hence we anticipate a greater number of organ donations utilising these systems. We report two cases with CA due to cardiogenic shock and were managed with ECLS. Organ donation under ECLS is feasible and, following differentiated donor diagnostics, can contribute to good transplant functional outcomes.

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Pancreas / Small Intestines

S13-04

Technical Failure After Pancreas Transplantation: Risk Factors For Early Pancreas Grat Loss - A Multivariate Analysis

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Introduction

Technical failure (TF) rates remain high after pancreas transplantation. More than 10% of all pancreas grafts continue to be lost due to technical reasons in the early postoperative phase. Various factors on the donor and recipient side are discussed as risk factors. Many organ offers are rejected by centres due to factors that have not been proven to increase the risk of technical failure.

Methods
We performed a bivariate and multivariate analysis to determine causes and risk factors for TF of pancreas grafts within 3 months postoperatively.

Results
Between 6/1994 and 12/2017, 513 simultaneous pancreas kidney transplants (SPK) were performed at our center. Of these, 77 (15.0%) grafts were lost due to technical reasons (thrombosis, leaks, infections, bleeding, pancreatitis). Thrombosis (48%) was the most common cause for TF. In the bivariate analysis, there were significant differences found for cause of death, duration of donor ICU-stay, P-PASS and PDRI. By multivariate analysis, only cause of death was a significant risk factors for TF of the graft. Thereby, a traumatic cause of death reduced the risk for a TF (RR= 0.612; p=0.04; CI 0.379-0.986). Not significant were donor and recipient age, body mass index, cold ischemic time of the pancreas graft, and donor resuscitation.

Conclusion
The only variable for which a relative risk of technical failure was calculated that was significantly different from 1 was the donor's cause of death. If the cause of death was traumatic, the risk of technical failure was 0.612 times greater (i.e. smaller) than for a non-traumatic cause of death.

Basic Science

S14-02

Bcl6 Inhibitors Potently Inhibit Allogeneic T Cell Activation - A Novel Mechanism Of Immunosuppression?

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Introduction
Bcl6 is a key transcription factor regulating T cell fate. We explored the potential of novel Bcl6 inhibitors (Bcl6i) as immunosuppressants in transplantation.

Methods
First, we determined Bcl6 expression in T cells in KTx biopsies (10 TCMR, 10 non-rejection) using multiplex immunofluorescence ISH. To test the effects and mechanism of Bcl6i on T cell activation, we performed mixed lymphocyte reactions (MLR) using healthy donor PBMC. Briefly, CFSE-labeled responder PBMC, or sorted CD4+ naïve (Tn), central (Tcm) or effector (Tem) memory T cells were cocultured with irradiated third party stimulator PBMC in the presence of different Bcl6i (79.6 or FX1), the Bcl6 degrader BI-3802, and the vehicle control. After 5 days, CD4 and CD8 T cell proliferation and expression of cytokines, granzyme B and perforin were measured. In addition, we tested Bcl6i action in PBMC from KTx patients with (n=9) and without rejection (n=7).

Results
Indeed, we found pronounced Bcl6 expression in T cells during TCMR. Next, we studied the immunosuppressive effects of Bcl6i, which potently inhibited proliferation and function (IFN-g, GrB, Perf) of CD4 and CD8 T cells compared to vehicle (max. 90% inhibition) without affecting viability. This appeared to be a class effect, since FX1, 79.6 and BI-3802 showed similar effects. Bcl6i interfered with early (d0-3) rather than late (d4-6) activation and Tn, Tcm and Tem were equally inhibited by Bcl6i. Q-PCR gene expression analysis indicated that Bcl6i affected T cell fate, since canonical Th subset markers were differentially regulated. To test whether alloreactive T cells from KTx patients would also respond to Bcl6i and be more responsive during rejection, KTx patients' PBMC were stimulated with donor cells. T cells from rejecting patients showed increased proliferation, Tcm and Tem subsets and cytokine (IFN-g, IL-2) expression than those from non-rejecting patients, but these parameters were significantly reduced by Bcl6i.

Conclusion
We found that Bcl6i potently inhibit the proliferation and function of T cells, especially during rejection. Since Bcl6 is markedly expressed by T cells during rejection, Bcl6i may have potential as novel immunosuppressants.

S14-03

Sex Hormones Impact Transplant Outcomes Through A Modified Dendritic (DC) - T Cell Communication

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Introduction
We previously demonstrated inferior death-censored graft survival in young female kidney transplant recipients. Conversely, graft survival was superior in older female recipients, suggesting an impact of sex hormones on alloimmunity. In this study we elucidate mechanisms underlying the effects of estrogens on DC and T cell interactions on single-cell level.

Methods
Female C57BL/6 (3-month) mice underwent bilateral ovariectomies (OVX) or sham surgery prior to MHC fully-mismatched heterotopic heart transplants. Grafts were procured at day 5 to assess morphology, immune responses, in addition to single-cell analysis CD45+ cells using scRNAseq on the 10X genomics platform. Data were analyzed using CellRanger and RStudio. Ex vivo validation included mixed lymphocyte reaction (MLR) and DC-T cell assays.

Results
Estradiol levels decreased significantly after OVX, leading to prolonged graft survival (10vs.8 days, $p< 0.05$) and reduced immune cell infiltration. Graft infiltrates by day 5 revealed decreased DCs (6.7%vs.14.1%) and Th1 T-cells (26.4%vs.37.6%), while Treg populations increased (18.0%vs11.2%; all $p< 0.05$). ScRNAseq identified sex-hormone specific cell clusters for monocytes, CD4 and CD8 T-cells, B cells, NK cells, NKT cells, neutrophils, and DCs. Tnfsf9, Il2, Il4ra, Cxcr4, Ccl17, and Il15ra expression was downregulated in Cst3+Ccr7+ DCs following estrogen deprivation, indicating inhibition of cytokine-cytokine receptor and co-stimulation pathways in DCs. A CD4 T-cell cluster with high expression of co-stimulatory and memory cell markers were also reduced after OVX, suggesting compromised antigen processing and presentation. Ex vivo coculture, of recipient's DCs with naïve CD4 T-cells after OVX confirmed compromised co-stimulatory DCs/CD4 T-cells interactions. In MLR, CD4 T-cells from OVX mice showed impaired proliferation, IFN-γ production, and increased cell death.

Conclusion
We report the first estrogen-dependent immune landscape at the peak of alloimmune response based on single-cell transcriptomic profiling. Our findings highlight the significance of biological sex in alloimmunity, emphasizing the necessity of sex-specific treatments in organ transplantation and beyond.

S14-04

Chronic Rejection Represents A Process Of Accelerated Aging That Can Be Treated With The Depletion Of Senescent Cells (SCs) And Their Senescence-Associated Secretory Phenotype (SASP)

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Introduction
Solid organ transplantation for end-stage organ failure falls short of its potential due to chronic rejection (CR). We propose that CR is driven by accelerated ageing, caused by SCs and their SASP. Our study explores the potential of senolytics combined with losartan to target SCs, SASP factors, and fibrogenic pathways.

Methods
MHC mismatched heterotopic heart transplants were performed in BALB/c to C57BL/6 mice. Recipients received immunosuppressive treatment with CTLA4-Ig. Chronic structural changes and alloimmune response were assessed by histology and FACS. Accumulation of SCs and SASP factors were evaluated using immunohistochemistry and RT-PCR. Recipients were treated with senolytics (Dasatinib+Quercetin), losartan alone or a combination of senolytics and losartan to target SCs, SASP products, and fibrogenic pathways.

Results
Chronically rejected cardiac grafts exhibited increased numbers of SCs with significantly elevated SASP levels (p21Cip/Waf; p16INK4a; SA-β-Gal positive cells; p16INK4a/IL-6 and p16INK4a/TNFα double-positive cells, all $p<0.05$). Senolytics depleted SCs and reduced SASP factors (p21Cip/Waf; p16INK4a; TNFα; IL6; all $p<0.01$). Vascular neointimal hyperplasia improved significantly ($p<0.01$), while progression of fibrosis was halted ($p<0.05$). Profiling systemic alloimmune responses after senolytic treatment revealed increased Treg, and decreased Th1 and Th17 cell numbers (all $p<0.01$). Within grafts, CD4+ T and CD8+ T cells, neutrophils, and macrophages were significantly reduced (all $p<0.05$). Senolytic treatment prolonged allograft survival significantly (MST=34.5vs.49.0days, $p<0.05$). Most notable, 75% of animals additionally treated with losartan survived >100 days, compared to 11% of control animals, with grafts showing reduced fibrotic remodeling.

Conclusion
Accelerated ageing plays a crucial role in chronic allograft dysfunction. Depleting SCs significantly improves graft morphology and prolongs graft survival. Targeting SASP factors and pro-fibrogenic and inflammatory pathways further improved outcomes. The combined treatment with senolytics and losartan holds promise as a novel and effective approach for treating CR in transplantation.

S14-05

Type 2 Innate Lymphoid Cells Protect The Renal Allograft Via The IL-33/ILC2 Pathway During Cold Ischemia Reperfusion Injury In Experimental Kidney Transplantation

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Introduction
Innate lymphoid cells (ILCs) do not express antigen-specific receptors, persist mainly in solid tissues and play a critical role in regulating inflammation and tissue homeostasis. Especially induction of ILC type 2 cells (ILC2s) by exogenous application of the alarmin IL-33 has been shown to mediate reno-protective processes upon ischemia-reperfusion injury (IRI). However, the role of ILC2s for homeostasis and improved graft function following kidney transplantation (KTx) remains to be defined.

Methods
We studied the renal-protective effects of ILC2s by applying a murine model of KTx.

Results
In a syngeneic C57BL/6 to C57BL/6 KTx setting, donor pre-treatment with recombinant IL-33 (300 ng/day) for 5 consecutive days prior to KTx resulted in a significant expansion of intra-renal ILC2s and protected the kidney against prolonged cold ischemia (6 hours) reflected by reduced tubular injury and significantly improved creatinine levels. IL-33 pre-treatment was less protective in Nmur1CreID2flox (ILC2-deficient) mice, supporting the kidney-protective role of ILC2s. Moreover, in the BALB/c to C57BL/6 allogenic transplantation setting with prolonged cold ischemic time under immunosuppression (CTLA-4 Ig), donor pre-treatment with IL-33 resulted in significantly improved graft function, thereby proving the effectiveness of this treatment. Of note, without co-stimulatory blockade, donor pre-treatment resulted in accelerated inflammation and graft deterioration indicated by elevated creatinine levels compared to controls. Furthermore, kidney-resident ILC2s of the donor are lost in this setting and although recipient-derived ILC2s infiltrate the graft already within 24 hours post KTx, these cells did not replenish the donor ILC2 pool and did not persist in the graft until day 7 post KTx. In contrast, recipient-treatment with IL-33 for 7 days post KTx resulted in higher renal ILC2 numbers than control-treated recipients but administration of IL-33 did not improve early graft function.

Conclusion
In summary, we report on the functional relevance of the IL-33-ILC2 axis in experimental kidney transplantation pointing towards a new regulatory cell type in this setting.

S14-07

Organ And Tissue Transplantation: Saving Not Only Money With Possible Scenarios For Germany

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Introduction
The transplantation of a much-needed organ, organs or tissue can save more than just one person's life. Firstly, we will compare the costs of dialysed versus transplanted patients for the health system. Secondly, we will present the results of our current survey among patients with chronic kidney disease before and during dialysis therapy. The costs for patients will be estimated by the quality of their social and professional life, as well as their general and mental health.

Methods
1. Comparison of the costs of dialysis and transplanted patients for the health system and ecology [3] [4] 2. The evaluation of the health and social impact on patients with chronic kidney disease before and after dialysis treatments will be based on our current survey aiming this target group [3]. 3. The evolution of the numbers of organ donation and transplantation will be driven from yearly reports of Eurotransplant and DSO. 4. For projections of the numbers of CKD and diabetes in 2040-2050 we will use among others the WHO reports [2]. 5. Evaluation and discussion of the possible political and structural outcomes of presented scenarios for Germany will be based on experiences of other countries.

Results
For the health system, the financial and ecological costs of dialysis are much higher than those of transplanted patients. The patients and their families carry the burden of their health situation on a social and professional level. The structural problems of the health system in Germany add a negative impact on the patients' situation. Not only their general health situation is difficult, but they also suffer under massive mental health symptoms going as far as suicidal thoughts.

Conclusion
With prognostics of at least two times more patients with CKD and diabetes by 2040-2050 new combined solutions other than the "Decision solution" currently in force in Germany are urgently needed on the political and structural level [1] There is no perfect solution, but the chosen solution will be legitimised by the positive effects of organs and tissues donation and transplantation numbers and thus saving the discussed costs of dialysis for the health system but most importantly saving the patients' health or even life and improving their quality of life.

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Liver IV – Varia

S15-03

The Influence Of Primary (PSC) And Secondary Sclerosing Cholangitis (SSC) As Indication For Liver Transplant On Individual Waiting List Outcome – A Multicentric Analysis Of The Eurotransplant Registry

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Introduction

Primary (PSC) and secondary sclerosing cholangitis (SSC) represent cholangiopathies that mostly result in irreversible structural liver damage and therefore play a relevant role as indication for liver transplant (LT) within the Eurotransplant (ET) network. However, scientific debates are ongoing whether the current allocation criteria consider both PSC and SSC patients on waiting list in equal measure. Aim of this study was to demonstrate the current real-life influence of these LT indications on the respective waiting list outcome by analyzing the largest, international cohort of PSC and SSC patients on LT waiting list within the ET registry so far.

Methods

Pseudonymized patient data of all patients with PSC and SSC listed for LT within the ET network from 2013 until 2019 were provided by ET and respectively collected. Accordingly, uni- and multivariate comparative analyzes regarding survival and several other variables specific for waiting list outcome have been performed with these data.

Results

1423 patients were included in this study. Of these, 1240 patients were listed for PSC, 183 for SSC. The ratio of SSC patients listed as „active" was significantly lower than in PSC (10.4% vs. 15.9%; $p<0.05$), even though median time on waiting list was comparable (SSC: 37.6 vs. PSC: 35.2 months). The fraction of patients dying whilst on waiting list was significantly higher for SSC than for PSC (21.3% vs. 8.4%), as was the velocity of these fatal occurrences (SSC: 18.8 vs. PSC: 28.5 months; each $p<0.01$). PSC patients were transplanted more frequently than SSC patients (63.8% vs. 59.0%; $p<0.05$), whereas transplanted SSC patients had significantly higher LabMELD values (18.0 vs. 13.8) and needed dialysis more often (5.6% vs. 0.9%; each $p<0,01$).

Conclusion

SSC patients suffer from significantly elevated mortality and reduced survival time on LT waiting list, as compared to PSC patients. One explanation might be elevated illness burden in SSC patients, yet another explanation might also be represented by the current allocation system which eventually favors PSC patients. These findings should be considered in center evaluations and lead to re-evaluation of the ET allocation criteria.

S15-04

Limited Access To Liver Transplantation And Tips Despite High Mortality, Healthcare Resource Use And Costs Of Liver Cirrhosis In Germany

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Introduction

Background and aims: Data on number of patients with liver cirrhosis in Germany are limited. We therefore aimed to estimate prevalence and incidence, comorbidities, mortality, utilization of health care resources, and costs of patients with compensated and decompensated cirrhosis in Germany.

Methods

This longitudinal observational study was based on an anonymized representative claims database including 4.9 million persons insured by a statutory health insurance (SHI) between 2015-2020. Patients with decompensated and compensated cirrhosis were selected via diagnostic ICD-codes and followed for two years.

Results

Prevalence of liver cirrhosis in 2015 was 250/100,000, resulting in 201,747 (95%-CI: 197,540-206,040) patients extrapolated to the German population. Out of all patients with compensated cirrhosis in 2015 who did not deceased, 16.0% developed a decompensation within three years. Overall, 978 patients (*Ø-age: 68 years; 60% male*) were included in the decompensated, and 5,135 patients (*Ø-age: 66 years; 59% male*) in the compensated cirrhosis cohort. Patients with decompensated cirrhosis had a higher burden of comorbidities (Charlson Comorbidity Index 7.3 versus 4.3) and 3-times higher costs per quarter (7,172€ versus 2,213€) than patients with compensated cirrhosis. 1-year mortality after decompensation was 51% compared to 8% in compensated liver cirrhosis. Of note, only few patients with decompensated cirrhosis received a liver transplantation or transjugular intrahepatic portosystemic shunts (TIPS) (1% and 5%).

Conclusion

Patients with cirrhosis have a high health care burden in especially decompensated stage. Accordingly, 1-year mortality of decompensated cirrhosis in Germany is high. Despite high health resource utilization, only few patients have access to liver transplantation or TIPS.

S15-06

Short- And Longterm Outcome After Early Allograft Dysfunction In Liver Transplant Recipients – A Retrospectiv Single Center Study Of 631 Patients From Hannover

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Introduction
Liver transplantation is the established procedure for the curative treatment of end-stage liver disease. The decreasing number of donors and the high incidence of early allograft dysfunction (EAD) due to the increasing numbers of extended criteria donors (ECD) remains a clinical problem. The aim of this work was to investigate the short- and longterm outcome of recipients with and without EAD.

Methods
Retrospective, unicenter, analyses based on data from adult patients undergoing deceased-donor liver transplant from January 2007 to December 2017. EAD was defined by one or more of the following criteria: (i) bilirubin ≥10 mg/dL on postoperative day 7; (ii) international normalized ratio ≥1.6 on postoperative day 7, and (iii) alanine aminotransferase or aspartate aminotransferase >2000 IU/L within the first seven days after transplant.

Results
A total of 631 patients were studied and 53.6% of recipients developed EAD. Recipient criteria showed no significant differences between the EAD and non-EAD groups. Donor ventilation time (5.2 vs. 4.5 days; p=0.013), graft weight (1834.39 vs. 1589.73g; p<0.001), donor BMI (27.38 vs. 25.83; p<0.001) and number of donors with ECD criteria (59.2% vs. 49.5%, p=0.018) differed significantly. Patients with EAD had a higher likelihood of post transplant dialysis (38.2% vs. 23.0%; p<0.001) or re-transplantation (16.0% vs. 4.6%; p<0.001). They also had higher mortality during ICU stay (16.8% vs. 5.7%; p<0.001) and significantly lower graft survival (98.0 vs. 116.0 months; p=0.005), but without a significant difference in patient survival (111.0 vs. 120.0 months; p=0.177).

Conclusion
EAD and non-EAD recipients differ in donor and not in recipient criteria.EAD has significant influence on the graft survival and the postoperative mortality but does not influence the patient survival.The high rate of EAD shows the need of innovative methods such as machine perfusion in order to reduce the EAD rate and improve the clinical outcome after liver transplantation.

Machine Perfusion

S16-05

Metabolic Protection And Clearance Of The Microvasculature By Integrated Controlled Oxygenated Rewarming And Normothermic Machine Perfusion Of The Kidney

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Introduction
Normothermic Machine Perfusion of the Kidney (NMP-K) is an advanced technique for ex-vivo organ preservation. Recently, a phase 1 clinical trial (NKP1) has completed recruitment and has demonstrated the safety and feasibility of the Oxford NMP-K protocol (oxNMP-K) for up to 24 hours prior to clinical transplantation. Evidence from other groups suggests that (1) controlled oxygenated rewarming (COR) might provide metabolic protection against ischaemia-reperfusion injury (IRI); (2) microvascular erythrocyte/ fibrin(-ogen) accumulations induced during cold storage and subsequent NMP-K contribute to graft injury; (3) cold acellular perfusion can mechanically clear the microvasculature. Here we report a modification to oxNMP-K intended to minimise both metabolic IRI and microvascular plugging.

Methods
oxNMP-K was adapted to include 1 hour of oxygenated acellular perfusion at 15°C, 1 hour of COR, and seamless transition to standard oxNMP-K. Pairs of porcine kidneys (n=8/group) were randomised between intervention and control (oxNMP-K without COR). Perfusion data were continuously recorded. Perfusate samples and biopsies were collected at regular time points. Urinary oxygen tension was monitored using an intraurethral probe. Results were compared to human data generated during NKP1.

Results
Consistent with previous reports, we observed higher vascular resistance, greater urine production, and lower perfusate NGAL in the intervention group. We found an unexpected and important interaction between COR, ionised calcium concentration, and vasoreactivity. In contrast to previous studies, we did not find any significant evidence of microvascular occlusive pathology. However, greater D-dimer release in the control group suggested that clearance of the vascular compartment is improved with the greater renal blood flow afforded by standard reperfusion.

Conclusion
COR affords protection from metabolic IRI but induces higher vascular resistance. Our data suggest that microvascular occlusive pathology is of less relevance in kidneys transplantable by standard criteria than previously thought. Further clinical studies incorporating COR at the start of NMP-K are warranted.

S16-06

Incidence, Risk Factors And Outcome Of Hepatic Necrosis After Liver Transplantation Following Alloraft Normothermic Machine Perfusion

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Introduction
Normothermic machine perfusion (NMP) has regained attention in the last decade and is increasingly used for liver allograft preservation. To date, there are no data on hepatic necrosis (HN) after NMP. In our collective, segmental HN was frequently detected as an incidental finding on postoperative computed tomography (CT) scans. The aim of the present observational retrospective single-centre study was to evaluate the incidence, risk factors and outcome of HN after NMP liver transplantation (LT). We hypothesised that HN would be significantly associated with allograft weight.

Methods

All patients who underwent LT after allograft NMP at the University Hospital of Münster between 10/2019 and 03/2023 were included. Patients receiving a biphasic CT of the upper abdomen within 30 days after LT were included and stratified according to the occurrence of HN (hepatic necrosis: HN; no hepatic necrosis: noHN). The primary outcome was death-censored graft survival at 30 days and 3 months. Secondary outcome measures included early allograft dysfunction (EAD), serum alanine transaminase (ALT) and aspartate transaminase (AST) levels at 7 days and 3 months after LT.

Results

91 of 116 patients who underwent LT after allograft NMP were included in the final analysis. HN was detected in 34 patients (37%). Donor age, BMI and ET-DRI were comparable between HN and noHN. Both, cold ischemia time and NMP time showed no significant difference. Mean liver weight was comparable between HN and noHN (HN: 1811 $\pm$ 492 g, noHN: 1669 $\pm$ 400 g; p=0.182) and was not significantly associated with the occurrence of HN. Interestingly, the occurrence of HN was not associated with EAD (p=0.366). Both, AST and ALT were found to be comparable between HN and noHN 7 days (p=0.345; p=0.815) and 3 months (p=0.775; p=0.408) after LT. Death-censored graft survival at 30 days (p=0.065) and 3 months (p=0.282) showed no significant difference.

Conclusion

While HN after NMP LT appears to be a frequent incidental finding, the occurrence of HN did not affect recipient outcome. The long-term effects of HN should be further investigated in future studies.

Psychosomatics

S18-04

High Level Of Psychosocial Adjustment In Patients On Ongoing Ventricular Assist Device Support – A National Multi-Center Study

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Introduction

Advanced heart failure therapies such as durable ventricular assist device (VAD) support require psychosocial adjustment for those affected. Since VAD implantation has become an established treatment strategy, a focus on psychosocial factors is needed [1], [2].

Methods

In a nation-wide, multi-center, cross-sectional study, we recruited 393 participants with ongoing VAD support (3mts-3yrs on device; clinicaltrials.gov ID: NCT04234230) [3]. Patient demographics, psychosocial factors (social support, anxiety, depression, and quality of life), and major adverse events (thromboembolic events, bleeding, driveline infections) were assessed.

Results

Overall, 85.8% of the sample were male; mean age 58.3 years (range 18-85). The majority of the sample (89.3%) reported normal to high perceived social support. Participants expressed symptoms of anxiety within the normal range (M=6.0$\pm$3.9), mildly elevated depressive symptoms (HADS: M=7.6$\pm$2.9; PHQ-9: M=6.2$\pm$4.7), and good quality of life (KCCQ: M=65.3$\pm$17.9). Higher per-

ceived social support was associated with lower levels of anxiety and depression, and higher levels of quality of life within our sample (all p<0.001). Driveline infection was the most prevalent adverse event (32.6%). Binary logistic regression models did not identify significant associations for the occurrence of adverse events and variables of psychosocial adjustment.

Conclusion

Our sample perceived high levels of psychosocial adjustment. High social support was associated with better outcomes in levels of anxiety, depression, and quality of life, demonstrating potential for the future development and evaluation of targeted multi-professional social support interventions including peer- and caregiver support [4], [5].

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Kidney IV – Management of Tumours and Vascular Complications

S20-04

Genitourinary Tumors After Renal Transplantation - Urgent Need For Awareness

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Introduction

Genitourinary tumors count to the most frequently neoplasias after solid organ transplantation. In order to ensure adequate cancer-screening for transplanted patients, statistics of the inhouse patient population of each transplant center is essential.

Methods

We performed a unicentric retrospective analysis of our own patient population with regard to the incidence of neoplasias after kidney transplantation (NTX) between 2010 and 2020. Hereby, we set a focus on renal carcinomas (RC), prostate carcinoma (PCA), urothelial carcinoma (UC) and testicular carcinoma (TC).

Results

Ninety-three of of 710 patients (13%) presented with a neoplasia after NTX.

In univariate analysis, age ≥56 years, a Charlson Index greater than 4, and a cancer history were significant risk factors (p</=0.001) for development of a neoplasia after NTX. In multivariate analysis, cancer history remained as the only independent risk factor.

Twenty-nine of the 93 NTx-patients developed genito-urinary tumors (about 30%). Five of 29 patients died due to genitourinary cancer (4 renal carcinoma, 1 urothelial carcinoma of the urinary bladder).

There were 14 renal carcinomas (11 in the native kidneys, 3 in the transplant). Tumors in the graft were no de-novo tumors but from the donor itself.

Nine prostate cancers (8 localized, 1 with lymph node metastases), 4 urothelial carcinomas (solely urinary bladder) and 3 testicular tumors (solely seminomas) occured.

The median age at diagnosis was 62 for RC vs 65 for PCA vs 64 for UC vs 42 years for TC.

The median time to development of post-transplant genitourinary cancer was 32 months for RC, 12 months for PCA, 48 months for UC, and 38 months for TC.

Conclusion
Genitourinary tumors, especially renal cell carcinomas, are one of the most common tumor entities besides skin and lymphoma after NTX. They require specialized urological therapy and persistent follow-up for patients. In particular, patients with a history of pre-transplant tumors are at increased risk after NTX. This underlines the importance of a careful urological evaluation of the patients already before admission to the waiting list and regular cancer screening after renal transplant.

Infectiology

S21-03

Fungal Infections In The Transplant Cohort Of The German Center Of Infectious Diseases (DZIF)

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Introduction
Fungal infections are a serious burden in the post-transplant setting. Hence, we aimed to provide current insights in the epidemiology, characteristics and clinical courses of fungal infections observed in a representative cohort of Caucasian renal transplant recipients.

Methods
This is a prospective multicenter study based on the transplant cohort of the German Center for Infectious Diseases (DZIF). The present analysis evaluates all probable/proven fungal infections occurring in adult renal allograft recipients transplantated between 04/2011 and 09/2022.

Results
96 fungal infections were identified in 73/1258 (6.7%) renal allograft recipients. Candida albicans (40.6%), Candida non-albicans spp. (26.0%), Aspergillus fumigatus (13.5%) and Pneumocystis jirovecii (13.5%) were the leading agents. Pulmonal infections were most common (35.4%), followed by fungemia, intra-abdominal infections, and mucocutaneous infections. 19 episodes (19.8%) required an ICU treatment. The overall mortality was 16.6%[7.8;35.0] mostly (83.3%) due to invasive Aspergillosis. The 12-month survival after infection

was 58.3%[18.6;78.7] for any patients diagnosed with invasive Aspergillosis. Fungal infected patients were characterized by an advanced age, higher donor age, higher percentages of deceased donations, delayed graft functions, and prolonged in-patient stay. 65.8% of patients with fungal infection had a history of bacterial infection. Cumulative-incidence rate in European Senior Program (ESP)-patients was almost tripled compared to non-ESP-patients (14.5%[9.5;22.1] vs. 5.8%[4.3;7.6]) and almost quintupled compared to recipients their allograft from a living donor (3.3% [1.9;5.7]). The difference was particularly marked focusing on Aspergillus fumigatus, stated in a decupled cumulative-incidence-rate compared to non-ESP patients. Aspergillus fumigatus was the most common fungal agent in ESP-patients.

Conclusion

Fungal infections are likely to become increasingly prevalent. Identified risk factors were recipient/donor age, deceased donation, delayed graft function and prolonged in-patient stay. Special attention should be paid to Aspergillus fumigatus, concerning its unfavorable outcome especially in ESP-patients.

S21-05

First Experiences With Organ Transplantation of SARS-CoV-2 Positive Organ Donors In Germany

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Introduction

The SARS-CoV-2 pandemic had a major impact on solid organ transplantation in many countries. A significant decline of performed transplantations was described e.g. in Spain and Italy. Until March 2022, SARS-CoV-2-positive organ donors were excluded from organ donation in Germany because of the uncertainty regarding the transmission of the virus from the donor to the recipients. First results from other countries indicated that organs from carefully selected SARS-CoV-2-positive donors can be transplanted with acceptable risk for the recipients [1], [2].

Methods

From February 25th 2022 to May 25th 2023 all SARS -CoV-2 positive donors from whom at least one organ was successfully transplanted to a recipient were identified. An organ donor was identified as SARS- CoV-2 positive, if at least one PCR test from the lower/upper airways was positive in the 14 days prior to organ removal.The follow-up was done within the framework of the vigilance and surveillance system of the German procurement organization (DSO). The follow-up period was 14 days after transplantation.

Results

During the study period, 256 organs (29 hearts, 7 lungs, 73 livers, 146 kidneys and 1 pancreas) were transplanted from 92 SARS-CoV-2-PCR-positive donors to 254 recipients. The follow-up was complete in 198 from 254 recipients (198/254; 78%). In none of the cases a transmission of the virus from the donor to any of the recipients was detected in a follow up period of 14 days. Three recipients were tested positive on the day of transplantation. Eight recipients died during the follow-up period (1 heart recipient, 6 liver recipients, and 1 kidney recipient). 31 recipients of kidney grafts (31/114; 27 %) showed delayed graft function. In all other recipients immediate organ function was good, there was no indication that organ function was negatively impacted by the SARS-CoV-2 infection of the donor.

Conclusion

These findings support the early experience from other countries that such organs do not pose a major immediate risk for the transplant recipients. Nevertheless a close follow-up is needed and experiences especially regarding lung transplantation with SARS-CoV-2 positive grafts are still lacking.

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Poster Presentations

Poster Session 01: Basic Science / Immunology

P01-01

Use Of The German National Transplant Registry And Obstacles On The Way To Improve Transplant Medical Care In Germany

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Introduction
The promising and patient-oriented organ transplantation faces a lot of critique stemming from e. g. the so-called transplantation scandal as well as challenges related to data privacy and regulatory requirements. In order to improve the critical attitude, the implementation of the Transplant Registry (Tx Registry) and the use of the data for research purposes are intended to promote aspects of sustainability, transparency, modernity and patient safety in the field of organ transplantation.

Focus
Collection and usage of Tx Registry data are associated with (I) an application-oriented implementation on the national healthcare market and (II) answering current research questions.

Methods
Continuous aggregation as well as use of medical transplant data require high standards of data protection and data quality. A structured organisation of data collection and data validation ensures the successful implementation of these requirements.

Results
The structure and organisation of the Tx Registry build the framework for a use-oriented implementation in the current health care system (I) with the combination of pseudonymised data from different data providers on the basis of a defined data structure (data set „Bundeseinheitlicher Datensatz").In addition to a successful design and setup, the Tx Registry demonstrates the high quality of

the data collected to date. The valid data form the basis for addressing various research questions such as aspects to be considered in an expansion of organ donation, prediction of post-surgical courses and survival time analyses (II). Aside from the high data quality, data validation also showed that not all available data sets have been submitted yet, which can be attributed to a high process variability in documentation within the different transplant centers.

Conclusion

The implementation and possible uses of the Tx Registry were demonstrated successfully.Potential for optimisation lies in the improvement of consent documentation and a broader use of transplant medical data for research purposes.

P01-02

Clinicopathological Scores With Optional Nephropathology For The Prognostication Of Outcome For Deceased Donor Kidneys In Eurotransplant

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Introduction

Decision about discard or acceptance of the rare and increasingly marginal deceased donor kidneys in Eurotransplant (ET) countries has to be made without solid evidence. We developed and validated flexible clinicopathological scores for the prognostication of delayed graft function (DGF) and 1-year death-censored graft loss (1y-gl) reflecting current practice of six ET countries including Croatia and Belgium.

Methods

The training-set was n=646 DGF and n=737 for 1y-gl, with test-sets n=158 and n=162, respectively. In step 1, stepwise logistic regression models including solely clinical predictors were applied to estimate the risk of each outcome. In step 2, risk estimates were updated for intermediate risk-percentiles with histological predictors. Results were compared to established Leuven, simplified Irish, Balaz and Port scores.

Results

Prevalence of DGF was 27% in the training- and 29% in the test-set; it was 9% and 8% for 1y-gl. Step 1 revealed an increased risk of DGF with increased cold ischemic time, donor BMI, recipient BMI, dialysis vintage, number of HLA-DR mismatches or recipient CMV IgG positivity. On training- and test-set, c-statistics were 0.673 and 0.708respectively. At a range between 18% and 31%, accuracy of DGF-prognostication improved with histology including number of glomeruli and Banff cv.

Risk of 1-year graft loss was increased in recipients with increased cold ischemic time, sum of HLA-A. -B, -DR mismatches and donor age. Comparing training- and test-set, c-statistics were 0.693 and 0.788, respectively. Accuracy of 1y-gl-prognostication marginally improved (c-statistics = 0.701 and 0.791) on the whole set with inclusion of Banff ct (ct0/1 vs. ct2/3). Overall, calibration was good at the training-, but moderate at test-set while discrimination was at least not inferior to established scores.

Conclusion

Our novel simple flexible scores with optional inclusion of time consuming and often unavailable expert nephropathology should deliver good results for clinical practice in ET, on a par with established, less simple scores.

Our scores should undergo further validation and adjustment for donation after cardiac death and the increasing use of perfusion pumps.

P01-03

Impact Of Conversion Of Twice-Daily Tacrolimus To Once-Daily Extended-Release Meltdose Tacrolimus On Cellular Immunity

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Introduction

LCP-Tacro [LCPT], a novel once-daily, extended-release formulation of tacrolimus, has a reduced C_{max} with comparable AUC exposure, requiring a ~30% dose reduction in contrast to immediate-release tacrolimus (IR-Tac). Once-daily LCPT in de novo kidney transplantation has a comparable efficacy and safety profile to that of IR-Tac with advantages in bioavailability and absorption. The present investigation intends to analyse the effects of conversion from IR-Tac to LCPT on phenotype and function of T-cells and B-cells.

Methods

20 kidney transplant patients treated by triple standard immunosuppression with a stable graft function undergoing a switch from IR-Tac to LCPT were included in this observational prospective study. We measured the main immune cell types and performed an in-depth characterization of B cell, dendritic cells and T cells including regulatory T cells of the patients before and 4 and 8 weeks after IR-Tac to LCPT conversion using multi-parameter flow cytometry. Additionally, we analysed T cells by assessing third-party antigen (Tetanus)-reactive T cells, which could be analyzed by restimulation with tetanus vaccine.

Results

Overall, we found no significant alterations following LCPT conversion for the most immune cell populations with a few cell populations showing quantitative increase. Thus, 4 weeks after conversion, more lymphocytes and regulatory T cells could be measured in the patients. These differences were borderline significant (p= 0.051 and p=0.08 respectively). Furthermore, we found significantly more regulatory T cells with a naïve phenotype ($CD45RA^+CCR7^+$). These alterations did not change again 8 weeks after conversion.

Conclusion

Here, we demonstrate first insights into the immune system changes occurred under IR-Tac to LCPT conversion therapy in kidney transplant patients. While phenotypic and functional characteristics of the most T and B cell populations did not change following conversion to the Tac dose sparing regime, we could observe an increase in the number of regulatory T cells in peripheral blood following IR-Tac to LCTP conversion, which might additionally contribute to the overall immunosuppressive effect.

P01-04

Propionic Acid Promotes The Expansion Of Regulatory T Cells In Patients With End-Stage Renal Disease But Not In Renal Transplant Patients

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Introduction

Patients with end-stage renal disease (ESRD) suffer from progressively increasing low-grade systemic inflammation, which is associated with higher morbidity and mortality. For transplant patients, an increased inflammation contributes additionally to the increased risk of transplant rejection and injury. Therefore, both patient population will benefit from anti-inflammatory effects. The present study intends to analyse the effect of the short-chain fatty acid propionic acid on the chronic inflammatory state and T-cell composition in ESRD and kidney transplant patients.

Methods

10 dialysis patients with ESRD and 18 kidney transplant patients under immunosuppressive standard triple immunosuppressive therapy consisting of tacrolimus, mycophenolic acid and prednisolone, received 2 × 500 mg propionic acid per day for 30 days. The cellular immune system was analysed before and after the propionic acid supplementation and 30-90 days thereafter as a follow-up. We measured the main immune cell types and performed an in-depth characterization of T cells including Tregs, B cells and dendritic cells. Additionally, we assessed the functional activity and antigenic responsivity by analysis of third party antigen-specific T cells after their stimulation by recall (tetanus vaccine) antigen.

Results

In ESRD patients, we observed an expansion of CD25highCD127- Tregs after propionic acid intake. In contrast, the same supplementation in transplant patients under immunosuppressive therapy did not result in any expansion of Tregs. Other immune cell populations were not influenced by propionic acid supplementation and the functionality of pathogen-reactive T cells remained unaffected in ESRD and transplant patients after propionic acid intake.

Conclusion

Our data suggest that dietary supplements containing propionate might have a beneficial effect on increased systemic inflammation in ESRD patients through Treg expansion. However, this effect was not observed in transplant patients, which could be explained by counteracting effect of immunosuppressive drugs preventing Treg expansion. Further studies are required to evaluate clinical and immunological long-term effects.

P01-05

Delayed Repertoire Dynamics In Kidney Transplant Patients With High Levels Of BKV

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Introduction
Reactivation of Polyomavirus BKV is a severe complication in kidney transplant patients that can lead to a graft loss. The virus is controlled by cellular immunity and modification of the immunosuppressive regime can improve the clinical course of the diseases. However, the underlying dynamics of the immune system remains unclear. Here, we performed in-depth analysis of T cell receptor repertoires in three selected groups of kidney transplant patients within a large multi-centre study.

Methods
Individual T cell clones have their own distinct T cell receptor, which can be assessed using next generation sequencing. Using this technology, we analysed the T cell dynamics in kidney transplant patients without BKV reactivation or any immunological or other complications within the first year (n = 10), and compared these to patients who experienced BKV reactivation with a low peak viral load (viral load < 3,000 BKV copies/mL; n = 10) and with a high peak viral load (viral load > 10,000 BKV copies/mL; n = 10) within the first 12 months. The selected groups were matched for age, gender, underlying diseases, and immunosuppressive therapy.

Results
We found, that the repertoire diversity decreased over time for transplant patients without BKV reactivation, whereas the repertoire in patients with high BKV load was all over the lowest within the first month, but the highest after 12 months. This change in repertoire diversity was caused by shift in frequency of non-expanded T cells (< 0.1% of the repertoire) to expanded T cells (1-10% of the repertoire). The dynamic of the CDR3 length was likewise found to be delayed in patients with high BKV load. Interestingly, there was no difference in the clusters size of similar, repeated T cells, indicating differences in the quantity rather than quality of the immune response.

Conclusion
Collectively, these data demonstrate difference in the underlying T cell dynamics in patients without BKV reactivation and with high BKV load. Further studies combining single cell sequencing and analysis of BKV-specific T cell repertoires can provide further information on antiviral defence and possible therapeutic targets to control BKV replication.

P01-06

Ex vivo Characterization Of Kidney Transplant Tubular Epithelial Cell Co-Stimulatory And -Inhibitory Molecule Expression During Inflammation

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Introduction
Direct allorecognition is generally regarded as a result of antigen presentation and activation of recipient T cells by donor professional antigen presenting cells. However, tubular epithelial cells contribute the vast majority of cells in the kidney transplant, and their contribution to alloreactions despite being targets of cytotoxic T cells is not well understood.

Methods
We collected urine samples of healthy donors, kidney transplant patients, and living donors of kidney transplants. Subsequently, we isolated and cultivated kidney

tubular epithelial cells. To ensure transplant origin, we characterized the cells of living donors and the respective recipients by chimerism analysis. After treatment with cytokines IFNγ, TNFα, IL-1β, IL-6, IL-17A, and IL-22, we performed a flow cytometric characterization of over 20 markers.

Results

Chimerism analysis of living donor and recipient pairs revealed a near total transplant origin of the cultivated tubular epithelial cells (median 100% donor origin, minimum 96%, n=6 living donor-recipient-pairs). Inflammatory treatment with IFNγ, TNFα, and IL-1β resulted in an upregulation of MHC-I and -II, costimulatory molecules CD40, CD70, ICAM-1, and ICOS-ligand, the immunomodulatory molecule HVEM and/or PD-L1. Other molecules, such as CD80/CD86, 4-1BBL, CD48, and CD58, only showed little expression and/or modification by inflammatory treatment. Treatment with IL-6, IL-17A, and IL-22 only caused minimal modulation of immunomodulatory molecule expression.

Conclusion

Human kidney transplant tubular epithelial cells can be isolated ex vivo and studied without invasive procedures. We used this tool to characterize the immunomodulatory potential of tubular epithelial cells under inflammatory conditions, which are present during ischemia-reperfusion injury and rejection episodes. Tubular epithelial cells express not only MHC-I, but also MHC-II and a multitude of important immunomodulating molecules. Thus, they can significantly contribute to the activation and modulation of alloreactive CD4+ and CD8+ T cells.

P01-07

EliSpot Five Colour Cytokine Release Assay – Immunomonitoring As Close To Physiological Conditions As Possible

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Introduction

Laboratory diagnostics in immunomonitoring evolved rapidly in the last decades and became an indispensable part in personalised medical treatment. Along with a rising number of detectable analytes, the complexity of the assay systems increased as well. With every additional step implemented in an assay protocol, i.e. purification, incubation, fixation and permeabilization, just to name some, the risk of artefacts increases and incorrect results can occur.

Methods

The EliSpot technology offers the unique opportunity of analysing functional cell response undergoing the whole process of protein maturation and secretion in contrast to the detection of early stage mRNA (PCR) or intracellular accumulation of cytokines (ICS). Furthermore, based on the immediate capture of secreted cytokines from the stimulated immune cells, no side effects based on metabolization during the stimulation process are influencing the assay results as it can happen for ELISA. The EliSpot system requires a simple density gradient PBMC isolation. These cells are stimulated with an antigen and no additional cell metabolism-changing compounds are needed. Within this assay, conditions are essentially identical to in vivo environment with minimum manipulation. Moreover, the EliSpot is a robust and easy to perform assay which does not require extensive laboratory equipment. Compared to ICS, one drawback of classical enzymatic and early two colour assays has been their limited number of cytokines which could be analysed at once.

Results
Stepping up in terms of multi parameter analysis together with the preservation of all advantages of the EliSpot Assay, a new five colour fluorescent EliSpot has been developed for the simultaneous detection of Interferon gamma (IFN-γ), Interleukin-2 (IL-2), IL-6, IL-17A and Tumor necrosis factor alpha (TNF-α) on single cell level. These cytokines are covering the whole spectra of different immune answers.

Conclusion
Additionally, to gain the maximal scientific output of this multi cytokine assays, a new software for the evaluation of results has been released. The new "Count Combination Tool" allows the user to display and export all possible analyte combination according to individual needs.

P01-08

Immune Regulation Via Cotransplantation Of Hepatocytes In A Heterotopic Heart Transplant Model In The Rat

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Introduction
According to the current state of medicine, the rejection reaction of allogeneic organs and the associated necessity of lifelong immunosuppression for transplant recipients represents a considerable restriction of their quality of life and expectations. For the liver, this seems to apply only to a limited extent, which is why the characterization of liver-specific tolerance has increasingly become the focus of transplantation immunological questions in recent decades. Both the cell type responsible for this and the mechanism behind it remain unknown. Recent publications describe the induction of $CD4^+$ $CD25^+$ $FoxP3^+$ regulatory T cells (T_{reg}) by hepatocytes as an underlying mechanism.

Methods
Our project aimed to further characterize the immunomodulatory effect by cotransplantation of allogeneic hepatocytes on graft survival and on cell populations and distribution of the recipient immune system using a heterotopic heart transplantation model in the rat. For this purpose, we performed heterotopic heart transplantation and simultaneous hepatocyte cotransplantation in a prolonged as well as in a rapid rejection model. This was followed by flow cytoemtric and immunohistochemical analyses. In addition, *in-vitro* experiments were performed to further characterize a potential mechanism.

Results
Our data show that cotransplantation of allogeneic hepatocytes significantly prolongs graft survival in a rapid rejection model, but no tolerance can be achieved. Analogously, using mixed lymphocyte hepatocyte cultures, we can demonstrate *in vitro* that allogeneic, syngeneic, as well as third lot hepatocytes exert an inhibitory effect on the proliferation of cocultured lymphocytes. Detection of cotransplanted hepatocytes *in vivo* is only successful until the third postoperative day, at which time a significant but only transient increase in T_{reg} population is also seen. Hepatocyte injection causes a conversion from an inflammatory to a regulatory subtype within the monocyte population.

Conclusion
In conclusion, cotransplantation of allogeneic hepatocytes seems to be a promising approach to regulate immune responses, although further insights are needed to induce tolerance and to clarify the underlying mechanism.

P01-09

Longitudinal Dynamics Of Soluble And Cellular Immune Mediators In Paediatric Liver Transplantation (pLT) Identified Cytokine/Chemokine Signatures Associated With Rejection-Free Survival

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Introduction
In the European multicentre "ChilSFree" study, we aimed to characterize longitudinal dynamics of soluble and cellular immune mediators during the first year after pLT and identify biomarkers associated with outcome.

Methods
Using Luminex-based multiplex technique, we measured 50 cytokines/chemokines, growth, and adhesion factors in recipient plasma at eight visits: before (V0), day 7/14/21/28 (D7/14/21/28), 3/6/12 months (3/6/12Mo) after pLT (n=244). Absolute cell counts and relative proportions of immune populations in patient blood (n=179) were quantified by flow cytometry.

Results
The longitudinal dynamics of soluble immune mediators (SIM) after pLT revealed major changes in plasma secretome over V0-D14. While the timing was dominant first, the SIM profiling identified several stable SIM signatures potentially linked to the recovery patterns of patients at later visits. One SIM signature was characterized by the absence of pro-inflammatory markers CXCL8/9/10/12, CCL7, SCGF-b, sICAM-1 reduced liver enzymes (AST, GGT), and rejection score and might be predictive for improved outcome after pLT. Furthermore, we found higher frequencies of $CD56^{bright}$ NK cells in the blood of the same patients, a cellular hallmark described in operationally tolerant patients. Of note, this special SIM signature was observed a few weeks after pLT and might represent an early biomarker for superior outcome over an entire year. The superior outcome of this subgroup could not be explained by clinical parameters and may represent a shared molecular characteristic of potentially tolerant recipients.

The longitudinal dynamics of immune cells revealed that absolute cell counts and proportions of myeloid cells peaked at D7, followed by a gradual decrease at later visits. Simultaneously, $CD4^+$ and $CD8^+$ T and $CD56^+$ NK cell counts were reduced at D7 but recovered at D21 with a further increase at 12Mo. The dynamics of T and NK cells but not B cells, granulocytes, and monocytes after pLT were affected by the age of the patients.

Conclusion
SIM blood signatures may act as biomarkers for outcome after pLT, paving the way to early adjustment of immunosuppression and improved therapeutic options.

P01-10

Longitudinal Dynamics Of SARS-CoV-2 Spike-specific Antibody Responses In Patients On Waiting List And After Lung Transplantation

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Introduction
Patients with end-stage lung diseases on the MHH waiting list for lung transplantation (LTx) have been vaccinated against the SARS-CoV-2 spike protein with usually three doses of the mRNA vaccine. Hence, they are supposed to develop robust immune responses when vaccinated prior to LTx without the influence of immunosuppression. Therefore, we hypothesized the induction of high spike-specific IgG levels and protection against SARS-CoV-2 infection and severe COVID-19.

Methods
Longitudinal plasma samples obtained pre (n=70) and post LTx (n=28) of WL-LTx patients was analyzed for spike-specific IgG by Luminex-based multiplex assays. The threshold for positivity was set separately for each spike domain based on the median MFI +2σ in a healthy, unexposed pre-pandemic control group. Patients with previous SARS-CoV-2-infection were excluded.

Results
95.7% of WL-LTx patients had seroconverted for either RBD-, S1- or S2-specific IgG pre LTx and still 92.86% were positive post LTx. Overall, S1-, S2- and RBD-specific IgG MFI values did not significantly differ between pre vs. post LTx. A subanalysis of matched plasma samples (n=25) revealed that 52% of the WL-LTx patients showed a higher IgG response pre than post LTx for all three spike protein domains and 28% showed even elevated antibody levels post LTx. Interestingly, S2-specific IgG MFI values were significantly elevated compared to RBD-specific IgG MFI values, both pre (S2 vs. RBD $p<0.0001$) and post LTx (S2 vs. RBD $p=0.0225$).

Conclusion
The majority of WL-LTx patients mounted high SARS-CoV-2 spike-specific IgG responses following vaccination pre LTx. Based on the more efficient antibody production against the S2-domain compared to RBD- and S1-domains, S2-specific IgG responses should be included also in the general evaluation of humoral immune responses to SARS-CoV-2. As expected, WL-LTx patients showed a superior antibody response to vaccination compared to LTx-recipients vaccinated only after LTx, which could even be maintained after LTx in some patients. Therefore, both patients on waiting list and LTx recipients may benefit from additional booster vaccinations after LTx.

P01-11

Heart-Associated Cytokine And Endothelial Patterns Dominate The Ischemia/Reperfusion Response In Recipients Of Combined Heart/Lung Transplantation In Comparison To Lung Transplantation

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Introduction
Organ-specific differences are discussed for ischemia/reperfusion injury (IRI) in cardiothoracic transplantation (Tx) but rarely compared directly in a clinical setting. Therefore, we compared a cohort of combined heart/lung transplants (HLTx) with cohorts of isolated heart (HTx) or lung transplantations (LTx), respectively, with respect to cytokines and endothelial markers in recipient blood and perfusates. Despite the evident clinical differences, our aim was to determine whether the microenvironment of HLTx patients would be rather related to HTx or LTx patients.

Methods
Blood plasma pre Tx, at T0, T24 and perfusion solutions of 5 HLTx, 24 HTx and 26 LTx patients were analysed for cytokines and soluble endothelial markers using multiplex assays.

Results
Early after transplantation at T0 and T24, HLTX and HTx recipients displayed significantly higher plasma levels of IL-6, CXCL8/IL-8, Ang-2, IGFBP-1, PAI-1 compared to LTx recipients that returned to baseline after three weeks. Identical kinetics with minimal changes were detected in the three groups for TNF, HB-EGF, EGF, PLGF, sFasL, TGF-a. Unsupervised cluster and principal component analyses clearly grouped HLTx and HTx patients together, separating LTx recipients apart with IGFBP-1, Ang-2, and PAI-1 as lead parameters (all $p<0.01$). In contrast, HLTx perfusates were grouped together with LTx and not HTx indicating that this compartment is dominated by the lung rather than the heart.

Conclusion
A direct comparison of combined heart/lung with isolated heart or lung transplantation revealed that the early systemic IRI response of HLTx recipients is, perhaps counterintuitively, dominated by heart-associated endothelial markers like IGFBP-1, Ang-2, and PAI-1 which groups them together with HTx patients. The difference between recipient blood and perfusates provides strong evidence for an organ-specific impact on IRI with distinct heart- vs lung-associated signatures.

P01-12

Impact Of Deceased-Donor Characteristics: Outcomes Of Donor Kidney Pairs Accepted For Transplantation

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Introduction

To support acceptance decisions in kidney transplantation, deceased-donor based scores are increasingly used. Yet, the performance of these algorithms remains moderate and the impact of donor characteristics is controversial.

Methods

We analysed 52 kidney donor pairs (104 grafts) transplanted in different individuals. Recipients were followed for up to 3 years. Poor function (three-month estimated glomerular filtration rate (eGFR) <30 ml/min) and early graft loss (EGF) were the primary discriminatory factor. We reasoned that a relevant impact of donor variables would result in a high concordance rate of graft failure.

Results

Graft loss was significantly more frequent in recipients with reduced function or failure of the partner graft (Log-rank: p=0.006, Figure 1). This difference remained significant when we adjusted for recipient age, PRA and wait time (Cox HR: 3,2; 95% CI: 1.06-9.83, p=0.03). Yet, there was no difference between rates of death with functioning graft (p=0.3). Relevant risk factors were donor- and recipient age, donor eGFR and HLA-mismatches.

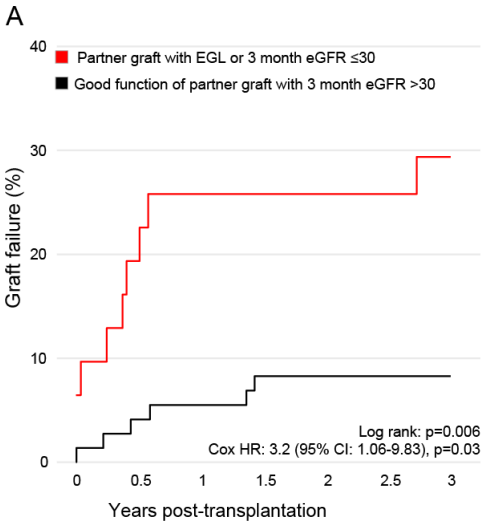

Figure 1 | Transplant outcome by partner graft function three months after transplantation. Cumulative incidence plots for graft failure **(A)** and death with functioning graft **(B)**. Red: Grafts where the respective partner grafts show eGFR ≤ 30 (estimated glomerular filtration rate in ml/min) or EGL (early graft loss) three months after transplantation, Black: Grafts where the respective partner grafts show good function three months after transplantation. Cox HR: cox hazards regression to adjust for recipient age, recipient time on dialysis, and previous immunisation (PRA>5%)

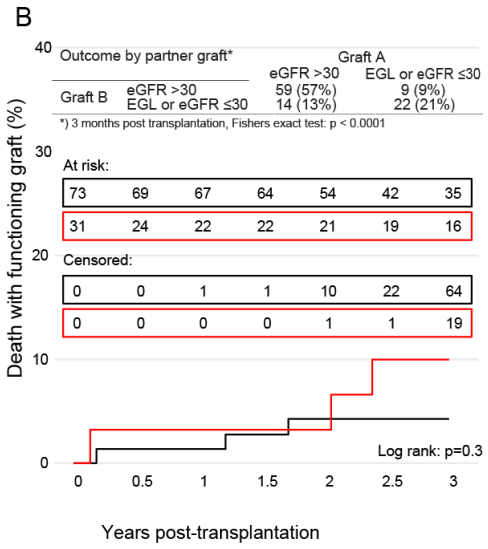

Figure 1 | (Continued)

Conclusion

Our results suggest that in kidney transplantation donor factors have a relevant impact on early transplantation outcomes. The use of donor-based clinical scores could potentially improve acceptance decisions and post-transplant outcomes.

P01-13

High-Risk Allele Mismatches Against HLA-DQB Increased The Risk For Adverse Outcome After Lung Transplantation

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Introduction
Human leukocyte antigen (HLA) mismatches between donor and recipient lead to eplet mismatches (epMM), which can induce the development of de novo donor-specific HLA-antibodies (dnDSA) and subsequently to allograft dysfunction. In particular, DQ-dnDSA are common after lung transplantation. The aim of our study was to identify risk factors for the development of DQ-dnDSA in relation to antigen and epMMs.

Methods
We included 187 non-immunized patients undergoing LTX between 2018-2020. All recipients and lung donors were typed for 11 HLA-loci. We monitored dnDSA with Luminex-based technology for one year post transplant. Number and type of epMMs were calculated with HLA-Matchmaker (OneLambda Fusion). The primary clinical outcomes of the study were acute cellular rejection (ACR) and chronic lung allograft dysfunction (CLAD).

Results
Out of 187 patients, 52(27.8%) developed dnDSA, and 42 (22.5%) patients developed DQ-dnDSA. DQ-epMMs were significantly higher among patients with DQ-dnDSA compared to patients without (p=0.0003). DQ-homozygous patients had a significantly higher risk of developing DQ-dnDSA than DQ-heterozygous patients (p=0.03). We found specific allele-combinations and thus high risk eplets (55PP, 55PPD, 66ER, 182N, 70RT, 45EV, 1667H, 66IL, 61FT, 84QL) that were significantly associated with the development of DQ-dnDSA. In the multivariate analysis DQ-dnDSA were significantly associated with ACR (p=0.03) and CLAD (p=0.01).

Conclusion
DQ-homozygosity, as well as high risk eplets lead to a higher risk of developing dnDQ-DSA. Therefore, detailed analysis of epMM would greatly improve the accuracy of immunlogic risk prediction before transplantation. Addressing these risk factors, for example by adjusting immunosuppression, could lead to improved long-term survival.

P01-14

Case Report: LVAD Support And Secondary Heart Transplantation Afterhematopoeticstem Cell Transplantation In Chronic Granulomatous Disease

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Introduction
Chronic granulomatous disease (CGD) is rare human inborn error of immunity (IEI) leading to functional defects of phagocytes and serious immunological deficiancies with inflammation caused by opportunistic pathogens and gastrointestinal complications [1].

Methods
Case report of a patient with CGD who underwent hematopoetic stem cell transplantation (HSCT) and secondary heart transplantation (HTx) following left ventricular assist device (LVAD) support by dilative cardiomyopathy (DCM) with multi-organ involvemen.

Results
Our case had several episodes of opportunistic infections in childhood as aspergillus pneumonias and stroke by septic embolism. In age of 14 y.o, HSCT was performed. After 10 years DCM with reduced ejection fraction (EF) was diagnosed. Coronarography showed coronary vessel disease. 5 years later EF deteriorated with a typical pattern of DCM. For persistent need of inotropic therapy the patient was listed high urgent (HU) for HTx. LVAD implantation was needed prior to HTX to stabilize hemodynamic situation. Recurrent bacterial infections and positive blood cultures occurred. PET-CT showed inflammation of the LVAD, thus leading to a second HU-listiung and initially HTx. The course was complicated by an ischemic colitis. Renewed infections after HTx, additional cytomegalovirus (CMV)

infection and progressive leukopenia aggravated the situation further. Bone marrow biopsy excluded hematologic disease. 1 year after HTx acute intestinal bleeding (AGIB), despite clipping, lead to resuscitation and sepsis by jejunal gangrene. CMV infection was reactivated. Aspergillus antigen was detected once. 4 months later a repeated AGIB caused an acute abdomen necessitating 3 laparotomies. Bronchoscopy revealed massive colonisation with Aspergillus fumigatus and CMV infection. The patient died in age 30 y.o,378 days post HTx after suffering an intracerebral bleeding.

Conclusion

Prevalence of IEI is underestimated [2] and has a potential multi-organ influence. The complex character of genetic mutations and altered immune response should be considered as a complicating factor in transplant medicine [5]. Aspergillus infection should be considered as potential coinfection in cases with recurrent CMV infections [3], [4].

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P01-15

Think Different: Improving Living Kidney Transplantation By Using Antibody Verified Epitopes

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Introduction

Previously, we reported the use of the next or third generation sequencing for the definition of HLA alleles, in the living donor set up in both adult and pediatric kidney transplantation (KT). Eleven loci are required since HLA antibodies are seen towards the products of these genes.

Methods

Patients (N=113) and their donors were typed by the next/third generation methodology. Antibodies were defined by Luminex SAB. Screening results were transcribed into antibody-confirmed epitopes using epregistry.com.br. The number of incompatibilities was calculated, and the data were used in case of re-transplantation.

Results

NGS increased the number of numerical MM by 64% for the loci A,B,C,DRB1,DQB1. For the additional typed HLA loci DRB345,DQA1,DPA1, and DPB1 we observed 2, 26, 3, and 23 MM, respectively. In total, 37.3% (69/185) of the de novo donor specific antibodies (DSA) formation was directed against these loci. Patients with biopsy proven antibody mediated rejection (ABMR), had a higher mismatch load when NGS typing was used. Then we transcribed the MM in epitope incompatibilities (EI), illustrated by the case: A 2-year-old boy with ARPKD on peritoneal received a kidney

from his grandfather. He returned to dialysis after graft failure due to humoral rejection. At the age of 13 years, he received a CDC xmatch negative postmortem kidney. Three weeks post-transplant the patient developed a biopsy proven acute ABMR. Epitope analysis revealed EI, shared between both donors (2 class I and 7 class II). The immunization against the 2nd donor, B*51:01 (epitopes 80I, 82LR) react against the A*24:02 of the primary donor. The B*51:01 allele of the 2nd donor shares the epitope 44RT (B*18:01) of the 1st donor. Detected de novo DSAs are targeted against these epitopes, suggesting sensitization during his 1st KT which remained undetected by the CDC xmatch beforen the 2nd KT.

Conclusion

This illustrates that definition of epitopes in patient and donor is a prerequisite for successful KT. Especially in pediatrics, this procedure will help to avoid undetected epitopes, which can trigger memory responses against the regraft. Defining epitopes facilitates the virtual crossmatch established recently.

Poster Session 02: Kidney Transplantation

P02-01

Characterization And 12-Month Outcome Of Living Kidney Donors In Germany – Results From The German Living Donation Register SOLKID-GNR (Safety Of The Living Kidney Donor-German National Register)

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Introduction

Living kidney donation (LD) represents the optimal treatment for patients with end-stage renal failure. The prospective National Living Donation Register SOLKID-GNR was established to provide clinical outcome data on living kidney donors (LKD) in Germany.

Methods
31 transplant centers in Germany evaluated LKD in an interdisciplinary approach. Clinical baseline data collected prior to and 12 months after LD were summarized to characterize LKD in Germany.

Results
626 LKD were enrolled (37% male, mean age 54 ± 10 years, range 28-83 years) representing 80% of the recruitable LKD in Germany. Pre-emptive LD was performed in 30.4%, AB0-incompatible LD in 26.4%, and 13.99% immunized LD with donor-specific antibodies.

Prior to LD S-creatinine was 0.81 ± 0.15 mg/dL and CKDepi eGFR 95 ± 13 mL/min/1.73m^2. Albumin/Creatinine ratio was 8 ± 20 mg/g; microalbuminuria showed 6.1% of the LKD. BMI was 26.1 ± 3.58 kg/m^2 (range 17-39 kg/m^2); BMI >35 kg/m^2 in 7 LKD.

Most of the LKD (80.83%) reported to be healthy. LKD reported to take regular medication for 25.8% hypertension, 0.6% diabetes, 8.6% hyperlipidemia, 3.9% sleeping disorders, 2.7% restlessness. 4.3% of LKD reported to have chronic pain, 4.2% cardiovascular diseases, 4.0% autoimmune/immunological diseases, 3.4% former malignancies, 5.4% psychiatric/psychosomatic diseases and 3.9% depressive symptoms; 3.1% LKD had psychotherapeutic support at the time of LD and 1 LKD reported fatigue symptoms prior LD.

For 270 LKD (43.1%) one-year follow-up data were available. 12 months after LD S-creatinine increased to 1.19 ± 0.24 mg/dL, and CKDepi decreased to 62 ± 13 mL/min /1.73m^2. LKD showed no obvious change in BMI, and blood pressure, but a slight increase of the rate of microalbuminuria (6.1% prior to 8.8% at 12 months). Physicians reported an increase of hypertensive medication from 25.6% prior to 31.6% 12 months after LD.

Conclusion
About 20% of LKD in Germany have/suffer from pre-existing medical condition. A 35% drop of renal function after LD and a risk for hypertension was confirmed. Structured regular follow-ups of LKD at the transplant center is mandatory to provide adequate medical care, especially in those already diseased.

The authors acknowledge the financial support by the Federal Ministry of Education and Research (BMBF/DLR; project number: 01GY1906) and the Medical Faculty of the University of Muenster.

P02-02

Physical And Mental Health Of Living Kidney Donors – Results Of The HeiKiD (Heidelberg Kidney Donor) Study

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Introduction
The aim of the present analysis was to provide detailed information concerning the clinical course as well as the physical and mental health of living kidney donors (LD) in the short- and long-term follow-up.

Methods
HeiKiDS (Heidelberg Kidney Donor Study) is a cohort study prospectively evaluating the demographic, medical and psychosocial situation of living kidney donors (LKD) at the transplant center Heidelberg since 2012. Here, we report on the results of the self-assessment questionnaires for health-related quality of life (SF-36) and fatigue (MFI-20) collected prior and in regular intervals after living donation (LD). In the present analysis LKDs with an at least 3-year follow-up were included.

Results
Altogether, 169 LKD were evaluated (59.2 male, age 53.3±18.5 years). 38.5% donated to their partner, 34.9% to their child. SF-36 and MFI-20 scores were in a favorable range compared to German general cohort results prior to donation. Kidney function decreased significantly with a 32% loss of glomerular filtration rate, but

kidney function was stable in the long-term interval. Fatigue scores (especially „general fatigue“ and „reduced motivation“) showed an increase, whereas physical and mental health scores slightly decreased over time, but remained in a good level compared to German general population. The main risk factors were pre-donation levels and donor age.

Conclusion
LKD showed a good mental health prior to donation. About 30% decrease in kidney function was confimed. Over time, fatigue scores and health-related quality of life scores worsened, mostly depending on age, but remained in a comparable level to the German general population.

We thank all participating kidney donors and the staff of HeiKiDS.

P02-05

440 Consecutive Hand-Assisted-Retroperitoneoscopic-Donor-Nephrectomies (HARP). A Comprehensive Analysis Of The Intraoperative Challenges And Potential Pitfalls

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Introduction
This analysis highlights the various pitfalls and challenges encountered in living kidney transplantation. This study aims to evaluate the outcomes and trends within an established living kidney program, providing valuable insights into the effectiveness and advancements in this area of transplantation.

Methods
A retrospective analysis was conducted on a cohort of living kidney transplant recipients who underwent transplantation at a specialized german transplant center between 06/2010 and 06/2023. Relevant data, recipient demographics, donor characteristics, surgical details, post-transplant outcomes, and long-term follow-up, were extracted from prospective database. Statistical analyses were performed to assess graft survival, patient survival. Complications were categorized in vascular, urinary tract associated, device- and donor associated pit falls.

Results
A total of 440 living kidney transplant procedures were included in the study. The mean age of the recipients was 52.8 $\pm$ 11 years, with a slight female predominance 58.5% female. All kidney grafts were taken out with hand assisted total retroperitoneous nephrectomy (HARP). 65% (286) were left kidneys. No conversion surgery had to be performed. Time of kidney explantation was 108.4 $\pm$ 27.9 min, time of the whole donation surgery 130 $\pm$ 27.5 min, warm ischemic time during kidney harvest was 122 sec $\pm$ 57, blood loss of the recipients was 49.2 $\pm$ 42 ml, 64 donors 16.4 % had multiple arteries and veins. In 228 (51.8%) cases potential pit falls were detected. 102 Vascular-(58.1%), 5 urinary tract- (2.2%), 46 donor-(25.9%) and 13 device associated pit falls (2.9%). If pit falls or deviating procedure were pointed out time of kidney explantation was longer 113 $\pm$ 28.52 p <0.001, warm ischemic time during kidney harvest was longer 143 $\pm$ 70 sec p <0.001 and blood loss was significant higher 60.1 $\pm$ 54.4 p<0.001.

Conclusion
The importance of blood loss, warm ischemia time, and operative time.By addressing these pitfalls, we can strive to improve the overall success and long-term outcomes of living donor renal transplantation and enhance the quality of life for transplant recipients.The importance of blood loss, warm ischemia time, and operative time.

P02-08

Induction With Low-Dose Thymoglobulin Vs. Induction With Simulect In Living Donor Kidney Transplantation

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Introduction
Induction therapy in living donor kidney transplant recipients with low immunological risk has been discussed controversially. Due to a change in our centre´s SOP for induction therapy, we can compare data from two recent cohorts in terms of efficacy and side-effect profile.

Methods
All recipients of living donor grafts between 3/2016 and 10/2021 who received induction with either thymoglobulin (ATG group) or basiliximab (Sim group) were included. Induction was performed irrespective of immunological risk. ATG was administered intraoperatively at 1.5 mg/kg/KG thymoglobulin. Further doses were administered on the first three POD according to the cellular immune status. In the Sim group, 20 mg basiliximab was given intraoperatively and on POD 4. Follow-up was 1 year.

Results
Thymoglobulin was administered to 70 patients with a median cumulative dose of 3.13 mg/kg. Induction with basiliximab was given to 61 patients. There were no significant differences in baseline demographics between the two groups. There were also no significant differences in post-operative complications such as urinary tract infection, pneumonia or post-operative bleeding. DGF occurred in 6 patients in the Sim group and in 3 patients in the ATG group (9.83% vs 4.3%, p=0.21). CMV or BKV viremia occurred in 16.4% and 16.4 % of patients in the Sim group and in 15.7% and 21.4 % of patients in the ATG group, respectively (p=0.91, p=0.47). No patient was diagnosed with PTLD. DSAs were detected in 10 patients in the Sim group and in 7 patients in the ATG group (16.4% vs 10% p=0.28). 18 patients in the Sim group and 11 patients in the ATG group had histologically proven rejection (p=0.058). Of the rejections in the ATG group, 10 were borderline. Only 12 out of 18 rejections in the Sim group were borderline. In addition to three humoral rejections, three cellular rejections were type IA, IIA and IIB.

Conclusion
This study demonstrated that low-dose thymoglobulin induction does not significantly increase the incidence of postoperative infectious complications. There was a trend towards a reduction in the number and severity of rejections after thymoglobulin induction, but this did not reach the significance level.

P02-09

Fixed Low Dose Versus Concentration-Controlled Initial Tacrolimus Dosing: Results From A Prospective Randomized Controlled Non-Inferiority Trial (Slow&Low Study)

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Introduction
Optimal initial tacrolimus (TAC) dosing and early exposure of TAC after renal transplantation (KTX) is not well studied.

Methods
In this open-label, multicenter, randomized controlled, non-inferiority study, we randomly assigned 432 renal allograft recipients to receive basiliximab induction, mycophenolate and steroids and either standard prolonged-release tacrolimus (trough levels: 7-9 ng/ml; arm A), or an initial 7-day fixed 5 mg/day dose of prolonged-release tacrolimus followed by lower tacrolimus predose levels (trough levels: 5-7 ng/ml; arm B). The primary end point was the combined incidence rate of biopsy-proven acute rejections (BPAR; including borderline), graft failure, or death at 6 months with a non-inferiority margin of 12·5%.

Results
The combined primary endpoint in arm B was non-inferior compared to the control arm A (22·1% versus 20·2%; difference 95% CI: 1·9- 8·8%). While overall rate of BPAR including borderlines were similar (B: 17·4% versus A: 16·1%, a statistically significant difference of higher than borderline graded BPAR was noted (B: 11·6% vs. A: 5·2%; p=0·027). Safety parameters such as delayed graft function, kidney function, donor specific HLA-antibodies, infections, or post-transplantation diabetes mellitus did not differ.

Conclusion
An initial fixed low prolonged release tacrolimus dose of 5 mg/day followed by lower tacrolimus exposure is non-inferior compared to standard tacrolimus therapy. For the first time in renal transplantation, therapeutic drug monitoring was abandoned within the first week and reduced tacrolimus trough levels were targeted later on. Within the different subgroups of this study, the initial tacrolimus fixed dosing approach appeared to be especially favorable for recipients at the age of 65 and older. It is a generally applicable, simplified, safe and effective immunosuppression approach that could replace the current standard drug monitoring accompanied by frequent dose changes.

(EudraCT-Nr: 2013-001770-19)

Funding
Investigator-Initiated Trial, financial support by Astellas Pharma GmbH

P02-10

Excellent Efficacy And Beneficial Safety During Observational Five Year Follow-Up Of Rapid Steroid Withdrawal After Renal Transplantation (Harmony FU Study)

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Introduction
We previously reported excellent efficacy and improved safety aspects of rapid steroid withdrawal in the randomized controlled one year "Harmony" trial with 587 predominantly deceased-donor kidney transplant recipients randomized either to basiliximab or rabbit antithymocyte globulin induction therapy and compared to standard immunosuppressive therapy consisting of basiliximab, low tacrolimus once daily, mycophenolate mofetil, and corticosteroids.

Methods
The five-year post-trial follow-up data were obtained in an observational manner at a three and a five-year visit only for those Harmony patients who consented to participate and covered clinical events that occurred from the second year onwards.

Results
Biopsy-proven acute rejection and death-censored graft loss rates remained low and independent of rapid steroid withdrawal. Rapid steroid withdrawal was an independent positive factor for patient survival (adjusted hazard ratio 0.554, 95 % confidence interval 0.314 to 0.976; p=0.041).

The reduced incidence of post-transplantation diabetes mellitus in rapid steroid withdrawal patients during the original one-year study period was not compensated by later incidences during follow-up. Incidences of other important outcome parameters such as opportunistic infections, malignancies, cardiovascular morbidity/risk factors, donor specific antibody formation, or kidney function did not differ during follow-up period.

Conclusion
With all limitations of a post-trial follow up study, the Harmony follow-up data confirms excellent efficacy and beneficial safety aspects of rapid steroid withdrawal under modern immunosuppressive therapy over the course of 5 years after kidney transplantation in an immunologically low-risk, elderly population of Caucasian kidney transplant recipients.

(Clinical trial registration number: Investigator Initiated Trial (NCT 00724022, follow-up study DRKS00005786)

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P02-11

Long-Term Kidney Function After Transplantation Within The European Senior Program – A Single Center Cohort Study

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Prospective Assessment Of The Need, Discrepancies, And Added Value Of Molecular Diagnostics Of Kidney Allograft Biopsies – An Evaluation In Clinical Practice

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Introduction
Kidney transplantation is the optimal treatment for end-stage kidney disease. The Eurotransplant Senior Program (ESP) aims to provide elderly individuals (≥65 years) with the benefits of organ transplantation. Given the scarcity of outcome data and risk assessment in this vulnerable population, this study examines results within the ESP.

Methods
This retrospective cohort study examined all kidney transplantations within the ESP at a single center performed between 2010 and 2021. Patients were followed until death, transplant failure, or end of the study period. Main outcomes were re-hospitalization within the first three months, 5-year patient and death-censored graft survival, as well as estimated glomerular filtration rate (GFR).

Results
158 recipients received 159 kidneys from 158 donors. Median follow-up was 3 years (interquartile range (IQR) 4). Donors had a median age of 72 years (IQR 8), with 51.9% being male and 16.5% having diabetes. Primary cause of death was non-traumatic cerebral hemorrhage (62%). Median creatinine at donantion was 0.9 mg/dl (IQR 0.4). Median graft cold ischemia time was 9 hours (IQR 6). Recipients had a median age of 70 years (IQR 8), with 70.3% being male, 24.7% having diabetes, and a median Charlson Comorbidity Index (CCI) of 5 (IQR 1). Three days after transplantation, median urine output was 1525ml/24h (IQR 1517). Delayed graft function occurred in 39.9%. At discharge, functioning grafts had a median GFR of 35ml/min/1.73m^2 (IQR 20.5), and the best GFR after transplantation was 43.5ml/min/1.73m^2 (IQR 25.5). Over the study period, GFR of functioning grafts remained relatively stable, with 35.5ml/min/1.73m^2 (IQR 22) after one year and 29ml/min/1.73m^2 (IQR 5.5) after ten years. 5-year patient and death-censored graft survival were 76% and 78%, respectively. Within three months of discharge, 66.5% were re-hospitalization.

Conclusion
This study demonstrates favorable long-term outcomes for kidney transplant recipients in the ESP. Transplant function remained almost stable over the study period with graft loss rates similar to non-ESP populations. These findings may contribute to the development of specific outcome prediction scores tailored to the ESP population.

Introduction
The Molecular Microscope Diagnostic System (MMDx) may resolve inconclusive histology findings, as preserved biopsy material can be examined after histology findings have been obtained. The extent to which this proposed approach can be implemented in clinical practice remains an open question.

Methods
We prospectively analyzed 102 consecutive indication kidney allograft biopsies by histology and MMDx at the University Hospital Zurich from April to September 2022. Pathologists and clinicians with experience in MMDx assessed the need for MMDx by questionnaire when the histology report was available. Clinicians then assessed the discrepancy rate and assumed added value by questionnaire when the MMDx report was available.

Results
The need for MMDx was most frequently assessed for suspected ABMR (12/20) and mixed ABMR/TCMR (9/18), but less frequently for proven ABMR (1/11), TCMR/borderline (1/6), DSA only (1/20), and no ABMR/TCMR (3/28). Discrepancies were observed most frequently in cases with proven/suspected rejection (36/55), but rarely in the

absence of histologic rejection (1/47). Clinicians considered an added value of molecular diagnostics mostly in suspected ABMR (3/20), mixed ABMR/TCMR (7/18), and TCMR/borderline (3/6). Classification into molecular ABMR occurred in 9 of 32 cases with suspected ABMR. However, classification into molecular TCMR was not observed in any of the 17 cases with suspected TCMR.

Conclusion

The need for MMDx in clinical practice goes beyond the recommendation for suspected ABMR. While discrepancies appear to be limited to cases with histologic rejection, an added value of MMDx is particularly suspected along the ABMR continuum. Because MMDx aims to overcome the inter-observer variability of histology, the potential added value of MMDx must be determined for each center individually.

P02-13

Isolated Glomerulitis Is Associated With The Absence Of Molecular ABMR in Cases With Histologically Suspected And Confirmed ABMR

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Introduction

According to the 2018 Banff classification, the Molecular Microscope Diagnostic System (MMDx) is indicated in cases when histology is insufficient to diagnose antibody-mediated rejection (ABMR) due to an absence of diagnostic criteria groups 2 (antibody interaction with tissue) and/or 3 (DSA and equivalents). The impact of isolated glomerulitis (g>0, ptc0) on the likelihood of molecular ABMR appears critical to the implementation of this new biomarker.

Methods

We analyzed 326 kidney allograft biopsies by histology and MMDx at the University Hospital Zurich from July 2021 to March 2023. Histologic findings were classified into: (1) 30 cases with suspected ABMR: isolated mild glomerulitis (g1), DSA-, (2) 32 cases with suspected ABMR: isolated mild glomerulitis (g1), DSA+, (3) 33 cases with suspected ABMR: MVI (g+ptc>1), DSA-, (4) 60 cases with confirmed ABMR: MVI (g+ptc>1), DSA+.

Results

MMDx diagnosed ABMR in 5/30 cases (17%) with isolated g1 without DSA, 12/32 cases (38%) with isolated g1 with DSA, 18/33 cases (55%) with MVI without DSA, and 30/60 cases (50%) with histologically proven ABMR. While only 17/65 cases (26%) with molecular ABMR showed isolated glomerulitis, 64/90 cases (71%) without molecular ABMR showed isolated glomerulitis ($p<0.001$). Among cases with isolated glomerulitis molecular ABMR was detected more frequently in cases with proteinuria ($p=0.011$), presence of DSA ($p=0.033$), and transplant glomerulopathy (cg; $p=0.014$).

Conclusion

MMDx confirms ABMR in a relevant proportion of cases with isolated mild glomerulitis. However, isolated glomerulitis is associated with absence of molecular ABMR in cases with suspected and confirmed ABMR. Presence of proteinuria, DSA, and transplant glomerulopathy is associated with molecular ABMR among cases with isolated glomerulitis.

P02-14

The Molecular Microscope Diagnostics System (MMDx) Does Not Identify Early Molecular ABMR In The Presence of DSA But Absence Of Histological Antibody-Mediated Changes

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Introduction
The development of de novo donor-specific antibodies (DSA) or an increase in MFI values of preformed DSA are common indications for kidney allograft biopsies. If changes in transcript patterns analyzed by the Molecular Microscope Diagnostic System (MMDx) may precede histological antibody-mediated changes and identify antibody-mediated rejection (ABMR), however, remains uncertain.

Methods
In this single-center cohort of 326 indication kidney transplant biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 138 cases with no glomerulitis (g0) and no ABMR (not meeting Banff 2019 ABMR criteria 1 and 2) concerning the presence (n=49) and absence (n=89) of DSA, and the presence (n=42) and absence (n=95) of double contours (cg).

Results
Kidney allograft biopsies in the presence of DSA were performed later post-transplantation (median 37 months (IQR 5-170) compared to biopsies in the absence of DSA (median 13 months (IQR 3-93; p=0.03). Molecular ABMR was observed in 0/49 cases (0%) in the presence of DSA and 2/89 cases (2%) in the absence of DSA (2 cases of mixed molecular ABMR/TCMR with histological TCMR). 17/49 cases (35%) in the presence of DSA showed an all ABMR rejection phenotype score (sum of R4, R5, and R6) ≥0.20 compared to 22/89 cases (25%) in the absence of DSA (p=0.116). 13/49 cases (26%) with cg showed an all ABMR rejection phenotype score ≥0.20 compared to 26/89 cases (29%) without cg (p=0.1). Among cases with cg, the all ABMR rejection phenotype score did not differ between cases with DSA compared to cases without DSA (p=0.294). 1/4 cases with isolated C4d positivity ≥2 in the presence of DSA showed an all ABMR rejection phenotype score ≥0.20.

Conclusion
MMDx does not differentiate molecular ABMR in the presence of DSA and/or transplant glomerulopathy but in the absence of histological antibody-mediated changes. If minor molecular changes are meaningful at least in a subgroup of cases, needs to be assessed in the context of follow-up biopsies.

P02-15

Five Scenarios Across The ABMR Continuum: The Added Value Of The Molecular Microscope Diagnostics System (MMDx) Confirmed By Follow-Up Biopsies

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Introduction
The Molecular Microscope Diagnostic System (MMDx) has evolved as an essential tool in antibody-mediated rejection (ABMR). However, cost and availability limit a generalized use making it even more important to outline specific scenarios, in which MMDx may add significant diagnostic value.

Methods
In this single-center cohort of 22 kidney allograft biopsies assessed by histology and MMDx, we analyzed (1) 5 cases with early active ABMR, (2) 2 cases with isolated glomerulitis, (3) 2 cases with microvascular inflammation (MVI) but no DSA, (4) 2 cases of MVI in ABO-incompatible (ABOi) transplantation, and (5) 2 cases with mixed rejection.

Results
(1) Two cases w/o DSA showed isolated glomerulitis (g1, ptc0, v0). On a follow-up biopsy one year later, histology no longer demonstrated glomerulitis and MMDx confirmed no rejection in each biopsy.

(2) Two cases showed MVI (g+ptc≥2) in the absence of DSA. On follow-up biopsy, histology showed ongoing MVI in one case confirmed by MMDx in each biopsy. On follow-up biopsy in the second case, histology showed no MVI (g0, ptc0) and MMDx confirmed no ABMR in each biopsy.

(3) Two cases after ABOi transplantation were diagnosed with TCMR plus MVI in the absence of DSA, confirmed by MMDx with molecular TCMR. After successful treatment of TCMR, MVI persisted on follow-up biopsy without any clinical suspicion for ABMR. MMDx showed no ABMR in each biopsy.

(4) In two cases with malcompliance, ABMR could not be diagnosed according to Banff with concomitant TCMR, but MMDx suggested ABMR/TCMR in both cases. After treatment for ABMR/TCMR, one case showed ongoing ABMR by histology and MMDx, while the other case showed resolved ABMR by histology and MMDx.

(5) One case showed no rejection on histology one week post-transplant, but minor ABMR by MMDx. On follow-up biopsy two weeks later, ABMR was confirmed by histology and MMDx. Four other cases with early active ABMR within the first two post-transplant weeks showed ABMR by histology and MMDx.

Conclusion
The MMDx appears to have added value across the ABMR continuum, both to confirm and reject the diagnosis of ABMR. Earlier diagnosis of early active ABMR, while possible with MMDx, seems likely to be the exception.

P02-16

The Molecular Microscope Diagnostics System (MMDx) Does Not Identify Molecular TCMR In Cases With Borderline Changes Or Isolated Intimal Arteritis In The Absence Of Microvascular Inflammation

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Introduction
Borderline changes suspicious for T-cell mediated rejection (TCMR) and isolated intimal arteritis (v-lesion) represent a particular challenge. Even though the Molecular Microscope Diagnostics System (MMDx) has not been trained on borderline changes and v-lesions, it has been suggested that MMDx may reclassify a subgroup of cases to molecular TCMR.

Methods
In this single-center cohort of 326 kidney allograft biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 153 cases with isolated tubulitis (i0, t1-3; n=114), borderline changes (n=10), and isolated intimal arteritis (i0, t0-2, v1; n=39) in the presence (n=81) and absence (n=72) of microvascular inflammation (MVI). 83 cases without histologic lesions

suspicious for TCMR (i0, t0, v0) were used for comparison of rejection phenotype scores. Any cases with overlapping pathologies were excluded from the analysis.

Results

41 of 81 cases (51%) with suspicion for TCMR and MVI showed molecular rejection (30 cases with molecular ABMR, 4 cases with molecular ABMR/TCMR (2 cases with isolated tubulitis, 1 case with borderline changes, 1 case with isolated intimal arteritis), and 7 cases with minor ABMR) compared to 6 of 32 cases (19%) without suspicion for TCMR but MVI (5 cases with molecular ABMR, 1 case with molecular ABMR/TCMR; p=0.003). However, 1 of 72 cases (1%) only with suspicion for TCMR, but no MVI showed molecular rejection (1 case with minor ABMR). No pure molecular TCMR was identified in any group. 11 of 153 cases (7%) with suspicion for TCMR showed a TCMR phenotype score (R2) ≥0.10 (7 cases with isolated tubulitis and 4 cases with isolated intimal arteritis) compared to 5 of 83 cases (6%) without suspicion for TCMR (p=1).

Conclusion

MMDx may identify molecular TCMR among cases with MVI irrespective of histologic suspicion for TCMR.MMDx does not identify molecular TCMR in cases with isolated tubulitis, borderline changes, or intimal arteritis without MVI. TCMR phenotype scores do not differentiate between isolated tubulitis, borderline changes, isolated intimal arteritis, or no histologic lesions suspicious for TCMR.

P02-17

Overlapping Pathologic Findings Other Than Rejection In The Kidney Allograft Biopsy: Pitfalls For The Molecular Microscope Diagnostics System (MMDx)

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Introduction

The Molecular Microscope Diagnostic System (MMDx) has been suggested to add diagnostic value in cases suspicious of antibody-mediated (ABMR) and T cell-mediated rejection (TCMR). Other overlapping pathologies, however, have the potential to mimic molecular rejection.

Methods

In this single-center cohort of 326 indication kidney transplant biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 66 cases with overlapping pathologic findings by histology: 15 cases with pyelonephritis, 21 cases with BK nephropathy (BKVN), 5 cases with granulomatous interstitial nephritis (GIN), and 28 cases with recurrent/de novo glomerulonephritis (GN).

Results

Pyelonephritis:5 of 15 cases (33%) with pyelonephritis showed minor molecular findings (normal rejection score but abnormal ABMR and/or TCMR score or vice versa), which were diagnosed in only 18 of 260 (7%) cases without overlapping pathologies (p=0.004). 8 of 15 cases (53%) with pyelonephritis showed a TCMR phenotype score (R2) ≥0.10.BKVN: 4 of 21 cases (19%) with BKVN showed minor molecular findings, whereas 3 (14%), 3 (14%), and 6 (29%) of 21 cases showed ABMR, TCMR, and ABMR/TCMR, respectively. 11/21 cases (52%) with BKVN showed an all ABMR rejection phenotype score (sum of R4, R5, and R6) ≥0.20, none of which had proven ABMR by histology.GIN: 3 of 5 cases (60%) with AIN showed molecular TCMR, of which 2 cases showed mixed ABMR/TCMR in the absence of any antibody-mediated changes by histology.GN: 21 of 28 cases (75%) with GN showed no molecular ABMR/TCMR, whereas 2 of 28 cases (7%) showed minor molecular findings, and 5 of 28 cases (18%) showed ABMR. Surprisingly, 16 of 28 cases (57%) showed an all ABMR rejection phenotype score ≥0.20, and 8 of 28 cases (29%) showed a late-stage ABMR score ≥0.20.

Conclusion

Minor molecular findings should always suggest the presence of any overlapping pathology. Cases of pyelonephritis, BKVN, and GIN mostly mimic molecular rejection and might be misleading in their interpretation. Although GN does not show molecular rejection in most cases, the elevated ABMR scores suggest a GN-associated phenomenon.

Poster Session 03: Liver and Pancreas

P03-01

Successful Interventional Occlusion Of A Chyle Leak After Lymph Node Dissection And Liver Transplantation For Unresectable Hepatoblastoma – A Case Report

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Introduction
Management of Hepatoblastoma (HB) is multimodal. Surgery remains the fundament of management and complete resection, potentially including lymph node dissection and liver transplantation (LT) is crucial for cure. Postoperative chylous ascites is the pathologic accumulation of chyle in the peritoneal cavity. It usually forms because of surgical trauma of the thoracic duct, cisterna chyli or major tributaries. Extended tumour resection and lymph node dissection are risk factors for postoperative chyle leak.

Methods
We present a case of a 4-year old girl suffering from postoperative chylous ascites following lymphnode dissection due to intrahepatic HB involving all liver segments, extensive lymph node and bipulmonal metastases.

Results
The patient underwent neoadjuvant chemotherapy. Residual pulmonary metastases were resected. Lymph node dissection in the hepatic ligament and interaorto-caval was performed. Still, major vascular involvement prohibited liver resection. LT evaluation concluded her to be a candidate for urgent LT. Upon laparotomy for LT, the abdominal cavity was filled with three litres of chylous ascites. LT was successful, but the girl continued to show a clinically relevant chylous fistula after return to a normal diet, preventing removal of postoperative drains and discharge from the hospital. MR lymphangiography revealed a chyle fistula in the right upper quadrant. Intranodal lymphangiography using ethiodized oil injection was performed. Ethiodized oil was also injected transcutaneous into the area of the suspected leak. The girl was set on a "medium-chain triglyceride" – diet for seven days. Clinical success was achieved and postoperative drains were removed shortly after uneventful return to a normal diet.

Conclusion
Conservative treatment with total parenteral nutrition is an effective but tedious treatment of chyle leak. When chyle leak is not resolved conservatively, only surgical treatment was considered to prevent serious complications. We present a safe and feasible alternative of interventional closure of abdominal chyle leaks with ethiodized oil injected into the lymphatic vessels or into the leak directly, if visible during lymphangiography.

P03-02

Successful Metastasectomy And Liver Transplantation For Unresectable Hepatoblastoma With Lymphatic And Bipulmonal Metastases – A Case Report

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Introduction
Comprising only one percent of all paediatric malignancies, Hepatoblastoma (HB) is the most frequent liver tumour in children with an increasing incidence and typically no underlying liver pathology. Stage and treatment depend on the degree of local tumour burden defined by the pre- and post-treatment extent of disease (PRETEXT or POST-TEXT). Surgery remains the fundament of management and complete resection is crucial for cure.

Methods
Here, we present a patient who underwent recurrent metastasectomy and curative LT as final surgical treatment of extensive, metastatic HB. Written informed consent was obtained from the patient's parents for publication of this case report.

Results
A 4-year old girl presented with intrahepatic HB involving all liver segments (PRETEXT IV), extensive lymph node and bipulmonal metastases. Explorative laparotomy confirmed irresectability; a tumour biopsy was taken. The girl was treated according to the SIOPEL-4 high-risk HB protocol, including cisplatin, carboplatin, and doxorubicin. A favourable response to therapy was seen, as shown by normalized serum AFP levels, regression of hepatic lesions, and metastases. Thoracotomy on either side was performed and eight lesions each were removed. Lymph node dissection in the hepatic ligament and interaortocaval was performed. No viable tumour cells were found. Still, major vascular involvement prohibited resection. Liver transplant (LT) evaluation concluded her to be a candidate for urgent LT. The girl underwent left lateral split LT. Adjuvant therapy with irinotecan and vincristine started one month postoperatively. At two months post LT, the patient showed excellent graft function without any complications or signs of malignancy.

Conclusion
All PRETEXT IV tumours and central PRETEXT III, particularly with vascular involvement, should be considered for LT after neoadjuvant treatment. Contraindications for transplant include lung metastases at presentation or extrahepatic disease. Performing thoracotomy or laparotomy to resect and biopsy residues after neoadjuvant treatment – provided no viable tumour cells are found – can be helpful in confirming eligibility for LT even in patients with metastatic disease.

P03-03

Influence Of TACE Treatment On The Development Of Arterial And Biliary Complications After Liver Transplantation In Patients With HCC

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Introduction
Transarterial chemoembolization (TACE) has an important role in bridging hepatocellular carcinoma (HCC) prior to liver transplantation (LT). According to current protocols, hepatic artery catheterization is performed every 4-12 weeks. The influence of the interventional procedure on possible arterial and biliary complications after LT is analyzed in this study.

Methods
The procedures and postoperative complications after LT in HCC were evaluated in a retrospective single-center longitudinal study. The cohort was divided into patients with TACE or TACE-naïve group with subsequent analysis of postoperative complications. The study was approved by the local ethics committee.

Results
The analysis includes 109 patients, of which 78 patients (n=62 male, median 62 years (range 32-75)) received TACE treatments (median n=3; range n=1-23). The median of the largest tumor diameter were 3.6 cm (range 1.1-14.0 cm) and 1.8 cm (range 0.4-11.9 cm), and the median number of tumor lesions were n=1 (n=1-5) and n=1 (range n=1-5) for the groups with or without TACE treatment, respectively. Patients received LT within Milan-In (n=49) or Milan-Out (n=17) criteria. Arterial complications were found in 8 patients (5 stenoses, 1 aneurysm, 2 dissections) or 1 patient (stenosis), as well as biliary complications in 14 patients (8 stenoses, 2 anastomotic leaks, 3 ischemic type biliary lesions (ITBL), 1 CAST (lithogenic material within the bile ducts)) or 11 patients (4 stenoses, 6 anastomotic leaks, 1 ITBL) in the groups with or without TACE treatment, respectively. Retransplantations were performed in 6 or 1 patient(s) (7% or 1%). There was no significant increase in arterial or biliary complications after TACE treatment (p=0.276 and p=0.075, respectively). In the subgroup analysis, we did not find any evidence of a more frequent occurrence of the investigated complications depending on the number of TACE treatments. In an in-depth assessment, we found, independent of TACE treatment, in 4 of 9 patients (44%) with arterial complications a pre-existing systemic vascular pathology.

Conclusion
The implementation of TACE treatments is not associated with a significant increase in arterial or biliary complications post LT.

P03-04

In Situ Hybridization And Multiplex Immunofluorscence Technology: A Novel Tool To Explore Immunological Processes In Liver Allografts

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Introduction
The mechanism of fibrosis onset in liver allografts with subclinical inflammation is widely unexplored. Assessing immunological processes in situ within single cells would represent a step forward to improve tissue diagnostics and treatment. Here, we present a proof-of-concept study using in situ hybridization with multiplexed immunofluorescence (mIFISH) to detect cytokines and perform cell phenotyping in formalin-fixed paraffin-embedded (FFPE) human liver tissue. The aim of the study was to validate mIFISH technology versus gold standard assays. In a second step we applied it to liver allografts to explore leukocyte activation, cytokine expression and periportal fibrosis.

Methods

FFPE tissue of NASH livers (n=3), non-NASH livers (n=3) and tonsils (n=3) were assessed for $CD45^+$ and CXCL9 with mIFISH, immunohistochemistry (IHC), chromogenic ISH (cISH/RNAscope) and qPCR. Liver allograft biopsies from six acute cellular rejection (rejection activity index (RAI) = 6-9), nine subclinical inflammation (RAI = 1-2) and six normal cases (RAI = 0) were labelled as follows: CXCL9.CD45.GZMB and TGF-β_1.CD68.αSMA. Quantitative analysis of histology was performed with an automatic machine-learning algorithm on whole-slide sections.

Results

mIFISH analysis strongly correlated with IHC for CD45 ($r = 0.99$, $p < 0.001$), with cISH for CXCL9 ($r = 0.99$, $p < 0.001$) and with mRNA expression levels detected by qPCR (CD45 $r = 0.78$, $p = 0.014$; CXCL9 $r = 0.82$, $p = 0.007$). Preliminary semi-quantitative analysis of mIFISH in subclinical inflammation showed similar CXCL9 expression levels as in acute cellular rejection. Expression of TGF-β_1 and periportal fibrosis was higher in subclinical inflammation than in normal cases (TGF-β_1p = 0.001, fibrosis p = 0,016).

Conclusion

The mIFISH assay is reliable compared to gold standard assays with the distinct advantage of being able to assess multiple immunological parameters within single cells. It may be a powerful tool to better understand subclinical allograft rejection in liver tissue.

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P03-07

Prognostic Value Of Soluble Urokinase Pasminogen Activator Receptor In Liver Transplant Recipients

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Introduction

Liver transplantation (LT) is a life-saving procedure for patients with end-stage liver disease. The identification of reliable biomarkers to predict long-term post-transplantation patient survival is crucial for optimizing patient care. This study aimed to assess the prognostic value of soluble urokinase plasminogen activator receptor (suPAR) in liver transplant recipients which has been shown to be a valuable predictor in several chronic and acute illnesses. However, data on suPAR in the context of LT are missing so fare.

Methods

We conducted a retrospective analysis in patients who underwent LT between 2002 and 2011. We analyzed samples at different time points including prior to transplantation, as well as at six, 12, and 36 months after transplantation. Plasma levels of suPAR were measured using suPARnostic® TurbiLatex (ViroGates, Birkerød, Denmark).

Results

In total, 318 samples of 85 patients were analyzed for suPAR levels. Median suPAR levels before LT (6.6 ng/ml (IQR 3.9-13.0)) were significantly higher compared to all time points after transplantation (6 months 4.7 (3.0-7.8), p<0.001; 12 months 4.3 (3.1-6.2), p<0.001; 36 months 5.2 (3.7-7.3), p=0.003; all ng/ml). SuPAR levels before LT were higher in long-term non-survivors compared to survivors (5.9 ng/ml vs. 6.7), however thedistribution did not differ significantly between both groups (p=0.802).

Importantly, suPAR levels at 12 months post-transplantation was found to be a predictor of 10-year patient survival in Cox-Regression (p = 0.001, Hazard Ratio(HR) = 1.215, 95% Confidence Interval (CI) = 1.080-1.366). In multivariate models this was found to be independent of patients' age, renal function and patients' sex (p=0.008, HR= 1.1.89, CI=1.047-1.351)

Conclusion

This study demonstrates that suPAR levels at 12 months after LT might serve as a valuable prognostic

biomarker to predict long-term patient survival. Increased suPAR levels at this time might contribute to identify patients at higher risk for adverse outcomes and enable targeted interventions to improve long-term patient outcomes.

P03-08

Association Of Torque Teno Virus Viremia With Histological Graft Injury And Immunosuppression After Liver Transplantation

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Introduction

Immunosuppression after liver transplant (LT) is guided by markers such as trough levels or drug doses, tolerability, and markers of graft injury (liver enzymes, surveillance biopsies, and liver stiffness measurements), but not by pharmocadynamic parameters of the immune system itself. Torque Teno virus (TTV) replication is controlled by immune status, reflecting the level of immunosuppression after solid organ transplantation. (1) TTV viremia (TTVv) has been associated with acute cellular rejection and infection within the first year after liver transplantation (LT). (2) Long-term data on TTV after LT and correlation with graft injury from protocol biopsies are limited.

Methods

We included 100 samples from 80 adult transplant recipients without replicating viral hepatitis who underwent liver biopsy (LBx) and plasma samples in the prospective LBx repository at our center between 2008 and 2019. (3) TTV DNA quantitation was performed by TaqMan real-time PCR.(4) TTVv was correlated with the degree of immunosuppression and histological data. Univariate and multivariate analyses were performed.

Results

The median time after LT was 23 months (range: 2-298). TTVv was detectable in 97%. TTVv correlated negatively with histological graft inflammation and fibrosis (LAF and Ishak scores) and positively with overall immunosuppression as quantified by an immunosuppression score, but not with dosages or trough levels of individual immunosuppressants. TTVv decreased over time after LT, particularly within the first year. The pharmacodynamic marker TTVv did not correlate with pharmacokinetic assessments of immunosuppression intensity (CNI trough levels or immunosuppressant dosages), our clinical gold standards for guiding immunosuppressive therapy.

Conclusion

The association of histological graft injury with lower TTVv highlights that a pharmacodynamic marker would be preferable to individualize immunosuppression after LT. However, the high variability of TTVv at the low doses of immunosuppression given after the first year precludes TTV as a clinically useful marker after LT.

We thank Konstantinos Iordanidis from the "immune tolerance working group" at Hannover Medical School for technical assistance in performing the experiments.

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P03-09

Good Outcomes Even After Repeated Pediatric Liver-Retransplantations: A Justified Procedure Even In Times Of Organ Shortage

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Introduction
Pediatric liver transplantations generally represent advanced surgery for selected patients. In case of acute or chronic graft failure, biliary or vessel complications a retransplantation (reLT) can be necessary. In these situations, massive adhesions, critical patient condition or lack of good vessels for anastomosis can be problematic.

Methods
Between 2008 and 2021, 208 pediatric patients received a liver transplantation in our center. Retrospectively, all cases with at least one retransplantation were identified and stored in a excel database. Indication, intra- and postoperative course and overall survival (OS) were analyzed.

Results
Altogether 31 patients (14.9%) were retransplanted. In 22 cases only one retransplantation was done, 8 patients received 2 retransplantations and 1 patient needed a fourth graft. Median age for primary transplantation, first, second and third retransplantation was 14 (range: 1-192 months), 60.5 (range: 1-246 months), 58.5 (range: 14-131 months) and 67 months, respectively. While bile duct atresia (42%) and acute liver failure (23%) represented the main indications for the primary liver transplantation, acute and chronic graft failure (1. reLT: 36%, 2. reLT: 38%), thrombosis of the hepatic artery (1. reLT: 29%, 2. reLT: 25%, 3. reLT: 100%) and biliary complications (1. reLT: 26%, 2. reLT: 37%) were the most frequent indications for retransplantation. OS was 81.8% for patients with 1 reLT, 87.5% with 2 reLTs and 100% with 3 reLTs.

Conclusion
Pediatric liver retransplantation is possible with a good outcome even after multiple retransplantations in specialized centers. Nevertheless, a carefully patient and graft selection as well as good preoperative conditioning are essential
.

P03-11

Risk Stratification And Survival In Patients After Liver Transplantation: The Role Of Right Heart Function And Dimension Assessed By Transthoracic Echocardiography

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Introduction

Liver transplantation (LTx) is often the only treatment strategy in patients with acute liver failure or end stage liver disease. Because of the donor pool limitation, a preoperative examination of cardiac function status is mandatory.[1] Various studies have shown the interaction between the presence of pulmonary hypertension (PH) and post-transplant survival respectively graft durability.[2,3] We retrospectively evaluated right heart data by transthoracic echocardiography (TTE) in the evaluation process for LTx to identify complementary risk factors.

Methods

We performed a single-center retrospective cohort study of patients that underwent LTx. All patients were evaluated according to current guidelines. The images were evaluated by two dimensional TTE focused on following parameters: right ventricle basal end-diastolic diameter (bRVEDd), tricuspid annular plane systolic excursion (TAPSE) and right atrial area (RAA). Based on current literature pre-specified cut-offs for abnormal values were assessed for: bRVEDd > 39 mm, RAA > 16 cm^2 and TAPSE < 18 mm. Time period between TTE and LTx was blinded. Follow up was between date of LTx and following three years.

Results

We evaluated 350 patients who finally underwent LTx (mean age: 55.71 $\pm$ 10.26 years, 71.1% male). Patients had a median MELD-Score of 15 (mean: 16.83 $\pm$ 8.75). In univariate Cox regression cut-offs for TAPSE (p: 0.248) and RAA (p: 0.265) were not associated with a statistically significant impact on mortality. However, for bRVEDd univariate analysis showed a significant result (HR: 1.975, CI: 1.091-3.576, p: 0.025) as well as log-rank in the Kaplan-Meier-estimate (Chi^2: 5.25, p: 0.022). In the following multivariable analysis, including several laboratory values, bRVEDd remained significant indicating independent influence on survival (HR 2.206, CI: 1.105-4.404, p: 0.025).

Conclusion

Analysis of right heart function and dimension was able to provide additional information concerning increased right heart stress and postoperative mortality in LTx already at the time of listing. This combination of findings provides some support that right heart dimension could become a prognostic value in assessment for LTx in the future.

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P03-12

Health-Related Quality Of Life (HRQOL) Over The Course Of Up To 30 Years Post Liver Transplantation (LTx) – A Long-Term Single Center Study

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Introduction

LTx stands as the only life-saving procedure for individuals suffering from end-stage liver disease, offering a promising life expectancy. Assessing HRQOL in patients

who have undergone LTx offers valuable insights into the non-medical implications of this major medical intervention. Herein we present the HRQOL data of patients up to 30 years following LTx from our transplant center.

Methods

Between 2016 and 2022 HRQOL was assessed in patients at the day of and at various intervals up to 30 years after LTx. Data were acquired using the 36-item short form health survey (SF-36), which patients filled in at the regular check-up visits at out transplant center. The SF-36, consisting of 36 items grouped into 8 distinct scales, is a broadly used and accepted tool to measure the multiple dimensions of HRQOL.

Results

A total of 2244 SF-36 questionnaires from 1192 patients were included in the analysis. Among these, 54.5% (n=669) were male and 37.5% (n=461) female. The majority of the observed patients were between 41-60 years at time of transplantation (54.9%; n=674; total range of age: 0-77years). Cumulative analysis of SF-36 scores of all age-groups revealed stable scores over time, with mean SF-36 scores of 44.2 (±24.2; n=83) at the day of, 62.0 (±20.8; n=195) within the first year after, and 61.7 ±22.0, 64.4 ±23.9, 61.8 ±23.0, 61.0 ±24.4, 64.1 ±23.0 up to 5, 10, 20, 30 or >30 years after LTx respectively. Patients transplanted in childhood (aged 0-18 years) presented with higher mean SF-36 scores (71.7; ±19.0; n=53) 10-20 years after LTx compared to patients aged 19-65 years (61.0 ±23.2; n=580) and >65years (59.8; ±23.4; n=17) at the time of LTx respectively ($p<0.05$). Patients claiming to be a member of a religious community presented with higher mean SF-36 scores 10-20 years after LTx compared to patients without religion (65.1 ±21.6; n=210 vs. 59.9 ±23.1; n=124; $p<0.05$). In comparison, living in a relationship did not affect HRQOL 10-20 years after LTx (62.8 ±22.9; n=400 vs. 62.7 ±21.6; n=73).

Conclusion

We herein present a unique dataset of the HRQOL in patients long-term after LTx. Our analysis shows, that HRQOL remains stable in the course >30 years after LTx in a selected patient cohort.

P03-14

Successful Weaning From Dialysis After Liver Transplantation Is Associated With Poorer Outcome Compared To Discharge With Ongoing Intermittent Hemodialysis

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Introduction

The scarcity of donor organs demonstrates the need to strive for long-term survival after liver transplantation (LT) to ensure a fair organ allocation. The aim of our study was to determine the reasons patients die after LT and to identify possible risk factors.

Methods

Postoperative complications after LT were evaluated in a retrospective single-center study. Statistical analysis was performed by Chi^2-test and Kaplan-Meier-estimates with log-rank comparison. P-value ≤ 0.05 was considered significant. The study was approved by the local ethics committee.

Results

From 2008 to 2021, 621 LT were performed at our institution with 56 retransplantations (thereof 30 during same hospital stay). Children < 14 years as well as patients with insufficient documentation or missing follow-up were excluded. A cohort of 451 patients was analyzed. Median age was 58 years (16-78 years). Of the cohort, 158 patients died after LT (35%) with a median

time after LT of 9 months (0-151), 10 patients died within 1 month after LT and 51 patients died during the transplant hospital stay (11%). Most common causes of death were infections (n=39) with pulmonal foci being the leading cause, malignant tumors (n=25), transplant organ dysfunction (n=19), cardiac disorders (n=12), and cerebral infarction (n=7). Multiorgan failure was found in 21 cases. As expected, dialysis is associated with a negative outcome after LT (p<.001). In detail, de novo dialysis just before LT (p<.001) and beginning of dialysis after LT (p<.001) significantly correlated with death after LT. Of note, discharge with ongoing dialysis did not correlate with deteriorated survival (p=.729). But, in the cohort of patients with continuous venovenous hemodialysis (CVVHD; n=147), survival was significantly better if patients were not successfully weaned from dialysis (n=36) but discharged with intermittent hemodialysis (IHD; p=.042).

Conclusion

Renal dysfunction remains a common complicating factor with vast impact on mortality before and after LT. In particular, the need for CVVHD after LT must be evaluated critically. Attempts to wean from dialysis should be considered amid the reported results of poorer survival compared to patients discharged with IHD.

P03-15

Influence Of Marginal Organ Factors On Drug Metabolism In Liver Transplantation - Perspective

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Introduction

Due to the lack of donor organs, there is an increasing use of non-optimal organs. These are organs from aged donors, with steatosis or grafts subjected to prolonged cold ischemia. Those factors might influence the recovery of function after transplantation and thereby affect outcome. One of the key functions of the liver is the drug metabolism. Ex-vivo assessment of drug metabolism includes the visualization of the key drug metabolizing Cytochrome P450 enzymes. For an improvement of the selection process of marginal organs, the CYP enzymes are used as a selective function parameter.

Methods

The impact of steatosis, the age and the cold ischemia time on CYP expression and activity before and after 1 hour of reperfusion is investigated. First, severity of steatosis as well as injury parameters are determined based on HE-staining of liver samples from transplantation. Second, CYP expression, reperfusion injury and tissue markers are visualized using the fluoremetic IHC multipanel method, which makes it possible to stain 6 targets on one slide. Third, CYP activity will be assessed using a fluorescent assay. As a fourth and thus clinical part, in-vivo assessment of CYP1A2 metabolism is performed using a breath test (LiMAx®) after injecting a test drug (Methacetin) accepted as a correlate of hepatic function. Samples from patients subjected to liver transplantation since January 2022 to May 2023 will be investigated and compared to the postoperative course.

Results

The CYP enzymes are expressed pericentral in the lobules. On POD 1 the LiMAx® shows a constant slop. On day 7 and 14 a baseline and a maximum are registered, illustrated in on clinical case so far. Steatosis, age, and CIT are three interrelated factors, that we predict, will influence the CYP expression pattern. We assume that the CYP activity is altered by the reperfusion and the IRI.

Conclusion

Potentially, the LiMAx® could be used to assess recovery after transplantation. The methods for measuring the CYP activity and expression are working. The next step is the use of donor samples and the correlation of CYP function as well as the IRI with the marginal organ factors.

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P03-16

Changes In TSP-1 Levels And Their Clinical Correlates In Liver Transplant Recipients

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Introduction
Thrombospondin-1 (TSP-1) is involved in various pathways including angiogenesis, tissue repair and wound healing. Upregulation in the extracellular space promotes pathological processes like inflammation or ischemia and leads to an overproduction of ROS. In the liver, TSP-1 has been shown to promote hepatocyte proliferation and migration. It is released by thrombocytes and interacts with integrin receptors on hepatocytes, initiating cell proliferation and survival. This suggests TSP-1 as an interesting target and prognostic marker in the context of liver regeneration.

Methods
In this prospective single-center study, a total of 22 patients who underwent deceased- (n = 15) or living donor liver transplantation (n = 7) between 11/2021 and 09/2022 at the Jena University Hospital were included in the analysis. TSP-1 concentrations were measured in the serum of the liver transplant recipients by ELISA preoperatively, during the anhepatic phase, after reperfusion and on postoperative days 1, 2, 7 and 14. More than 2000 clinical parameters such as cold ischemia time and the laboratory values were considered in the analysis of clinical data and collected using an SQL database.

Results
The mean age of the recipients was 56.99 years, with the youngest recipient being 33 years old and the oldest being 74 years old. Donors were slightly older, with a mean age of 61.12 years. The youngest liver donor was 39 years old and the oldest was 87 years old. We observed a statistically significant change in TSP-1 concentration over time. On average, the highest concentration was observed during the anhepatic phase. Younger liver transplant recipients and donors had higher levels of TSP-1, but these did not reach statistical significance. Patients who received a donor organ with a short cold ischemia time had significantly higher TSP-1 levels compared to patients with a longer cold ischemia time. Liver transplant recipients with longer operation times and hospital stays had significantly higher TSP-1 levels.

Conclusion
This suggests a possible role for TSP-1 in influencing the healing process after surgery, leading to delayed wound healing and complications that may require longer hospital stays.

P03-17

Thymoglobulin® Versus Grafalon® As Induction Therapy In Simultaneous Pancreas-Kidney Transplantation - A Monocentric Matched-Pair Analysis

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Introduction
Currently, a quadruple immunosuppressive therapy consisting of a T-cell-depleting antibody for induction, a calcineurin inhibitor, an antimetabolite and steroids is the gold standard in pancreas transplantation. There is a large variance in the choice of preparations as well as their dosages and target levels. The influence of the choice and dosage of the preparation on the success and safety of simultaneous pancreas-kidney transplantation is unclear.

Methods
A retrospective analysis of two patient groups was carried out using matched-pair analysis (n=72). One group received Grafalon® as induction therapy, the second group Thymoglobulin®. The primary endpoint is pancreatic graft function defined as freedom from insulin 12 months postoperatively. Secondary endpoints are postoperative complications, bioptically confirmed rejections, the detection of donor-specific antibodies and the occurrence of infectious diseases.

Results
Pancreas graft survival showed a 3 (6;12) -month survival of 83.3% (86.1%; 86.1%) in the Grafalon® group vs. 83.3% (77.8%; 75%) in the Thymoglobulin® group with a p-value of p=1.000 (p=0.630; p=0.485). Kidney graft survival showed a 3 (6;12) -month survival of 91.7% (83.3%; 83.3%) in the Grafalon® group vs. 94.4% (91.7%; 91.7%) in the Thymoglobulin® group with p-values of p=1.000 (p=0.565; p=0.586). The Grafalon® group showed significantly more frequent rejections (p<0.001), here the cellular rejections were significantly higher (p<0.001). The occurrence of humoral rejections was not significantly different (p=0.085). There were no significant differences in postoperative complications (p=0.729) and CMV infections (p=0.254).

Conclusion
While there were no significant differences in patient and graft survival as well as postoperative complications, we found significant differences in rejection free survival in favour of the Thymoglobulin® group. To point out graft survival and graft function were not influenced by this. The main limitation is the low Grafalon® dose (9mg/kg cumulative dose) and a possible bias in the biopsy rate. A prospective study is necessary to secure the results.

P03-18

Partial Nephrectomy For A Renal Cell Carcinoma In A Transplant Kidney After Simultaneous Pancreas-Kidney Transplantation: A Case Report

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Introduction
Simultaneous pancreas–kidney transplantation (SPK) is the preferred treatment for type-1 diabetes with end-stage renal failure[1]. However, solid organ transplantation (SOT) recipients are more susceptible to developing post-transplant cancers including renal cell carcinoma (RCC)[2]. Reports of malignant disease in renal graft after SPK transplantation are scarce, however the incidence of RCC is up to ten times higher in kidney only transplant recipients.

Methods
We present the case of a 54-year-old male who underwent successful partial nephron sparing graft nephrectomy 14 years after SPK transplant. A routine CT scan was performed due to decreasing renal function and revealed a 4.3 cm cystic lesion on the transplant kidney's upper pole and a 3.1 cm interpolar complicated cystic lesion with both partial solid component and enhancement on the arterial scanning phase. Following a review of the case by a multidisciplinary team, it was agreed to do an open partial nephrectomy.

Results
Surgery was performed as a joint case by urology and transplant surgery. The transplant kidney was fully mobilised after a midline laparotomy and adhesiolysis,

and the right common iliac artery, lower IVC, and both common iliac veins were slung as proximal vascular control. A second incision was made in the right groin parallel to the inguinal ligament, and the right femoral artery and vein were slung for distant control. The interpolar renal mass was entirely excised after intraoperative ultrasonography was used to visualise and demarcate the malignancy. The upper pole lesion was determined to be benign. The histopathological examination of the removed tumour and one common iliac lymph node revealed a pT1a pN0 ISUP grade 3 papillary renal cell carcinoma. The patient experienced a full recovery with preservation of renal function.

Conclusion

Papillary RCC appear more prevalent in transplanted kidneys as compared in native kidneys[3]. In our case, the patient underwent a successful complex organ-sparing procedure which turned out to be curative. The management of such unique cases should be carefully planned, and patients meticulously counselled as at risk of graft function loss and potentially high risk of mortality.

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Poster Session 04: Heart / Machine Perfusion

P04-01

A Case Series Of Cardiac Amyloidosis Patients Treated With Heart Transplantation Or Durable Mechanical Circulatory Support: Is The Surgical Approach A Legitimate Option?

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Introduction

Cardiac amyloidosis (CA) is a severe form of restrictive cardiomyopathy than can lead to progressive heart failure (HF) with high mortality. Heart transplantation (HT) and ventricular assist device (VAD) can be implemented in highly selected cases. There is still limited experience in surgical strategies for advanced CA and long-term results. We aimed to share our experience in surgical treatment of advanced CA after establishing an academic interdisciplinary CA program.

Methods
From 2020 to 2022, 6 patients (AL n=5, ATTR n=1) underwent surgery of advanced HF due to CA. Baseline, outcome, and follow-up were evaluated.

Results
4 cases received HT (n = 3; AL, n = 1; ATTR) and 2 VAD (n = 2; AL). Mean age was 58 (HT 61, VAD 56), and 5 were male. Diagnosis to surgery time was 15 (1,5-40) months. Prior surgery, diastolic dysfunction grade III (n = 6), reduced LV-function (n = 6), mean ejection fraction 40%, GLS of -8%, enddiastolic diameter (EDD) 44 mm, right EDD 39 mm in HT and 14 %, -5%, 63 mm, and 45 mm in VAD were recorded. INTERMACS score of 6 (n = 3; 2 HT, 1 VAD), 3 (n = 2; 2 HT), and 1 (n = 1; 1 VAD) was noted. All AL-CA achieved at least partial hematologic remission prior to listing. All HT were of high urgency and survived postoperative admission (mean ICU: 17 days). HT follow-up of 10 (3-23) months presents a 100% survival, no major complications, one acute rejection episode (1R ISHLT) in 2 HTs and no CA-recurrence. Patients with AL-CA received anti-plasma cell therapy post-HT. In this series, VAD served as destination therapy. Both VADs had multiple extracardiac involvement, needed prolonged ICU stay (44 days), ventilation (18 days) and died in-hospital. The most critical case (INTERMACS 1) received VAD as an ultima ratio concept, suffered cardiac arrest, acute right-HF with right-side VAD support, abdominal complications, and died after 27 days. The other VAD (INTERMACS 6) suffered intestinal bleeding and died of Covid19-ARDS after 51 days.

Conclusion
For carefully chosen patients, HT is a safe and promising approach. Further investigation is needed to highlight the benefit over risk in critical CA patients, and the ideal surgical approach to achieve best long-term results.

P04-02

Preoperative INR Does Not Predict Resternotomy In LVAD Patients Undergoing HTx

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Introduction
In patients with advanced heart failure eligible for heart transplant (HTx), left ventricular assist devices (LVAD) can be used as bridging therapy until an appropriate donor organ is available. To prevent device thrombosis and thromboembolic events, all LVAD patients require anticoagulation. Outside the clinic, this is achieved with vitamin K antagonists. As most listed LVAD patients are home before HTx, the majority arrive at the clinic fully anticoagulated with International Normalized Ratio (INR) of 2 to 3. Higher preoperative INR is a risk factor for major bleeds and mortality in other surgical fields [1], but its impact in LVAD patients undergoing HTx is largely unknown [2].

Methods
This single-centre retrospective study included all LVAD patients with HTx from May 2011 to March 2023. Anticoagulation reversal at HTx was performed with 10 mg of intravenous vitamin K1 and weight-dependent dosing of prothrombin complex concentrate based on in-house protocol. Spearman's rho, Receiver Operating Characteristic (ROC) curves and multiple logistic regression were used for correlation analyses. Significance was set as $p < 0.05$.

Results

138 patients (mean age 56.1 years ± 10.6; 81.2% male) were included. Mean preoperative INR was 2.4 ± 0.7. 81.9% of patients had an INR of 1.8 or more, with 63.1% in the target range of 2.0 to 3.0. Preoperative mean activated partial thromboplastin time (aPTT) and platelets were 38.9 sec ± 9.4 and 237.2 x 10^9/L ± 85.1, respectively. Mean preoperative haemoglobin was 11.7 g/dL ± 2.1. 39 patients (29.5%) required resternotomy. INR was not associated with resternotomy (AUC 0.52, p=0.35), 30-day mortality (AUC 0.44, p=0.75), 3-month mortality (AUC 0.52, p=0.39) or 1-year mortality (AUC 0.45, p=0.79) in ROC curve analysis or multiple regression, adjusting for aPTT, platelets and haemoglobin. Higher INR was not associated with more transfused red blood cells (RBC) (Spearman's ρ=0.14, p=0.12). Preoperative aPTT, platelets and haemoglobin were not associated with any of the outcomes measured.

Conclusion

Preoperative INR is not associated with resternotomy, mortality or transfused RBC in LVAD patients undergoing HTx, assuming appropriate anticoagulation reversal.

We would like to thank all our patients.

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P04-04

Rapid Progression Of Right Ventricular Failure In A Patient With Pulmonary Arterial Hypertension (PAH) And SOX17 Mutation - A Case Report

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Introduction

Right heart failure is the end-stage of PAH requiring rapid evaluation for heart and lung transplantation. Early manifestation of severe symptoms, sudden clinical deterioration and objective evaluation of disease severity possess a prognostic role. Through this case report, we want to present a rare case of acute right heart failure caused by a rapid progression of PAH.

Methods

A 19-year-old woman presented to our heart failure unit with dyspnea, syncope and cardiogenic shock. She reported the presence of recurring hemoptysis in the past six months. The ECG showed sinus tachycardia and no signs of acute ischemia. The blood tests showed massive elevation of NT-proBNP and TnT. The physical exam presented signs of volume overload. TTE showed typical features of cor pulmonale and severe tricuspid regurgitation. Peak systolic pulmonary pressure measured 105 mmHg+ZVD. A CT scan demonstrated signs of congestion and no evidence of pulmonary embolism. A lung ventilation-perfusion (V/Q) scan presented no typical aspects of mismatch. Advanced evaluation of pulmonary hypertension revealed a mutation in the SOX17 gene. Right heart catheterization showed aspects of severe pulmonary hypertension with increased pulmonary

vascular resistance and negative vasoreactivity testing (epoprostenol i.v.).

Results
The patient was treated with milrinone, epinephrine and inhaled iloprost. Our Heart Team carried out an immediate heart and lung transplantation evaluation and opted for high urgency status according to EUROTRANSPLANT guidelines. Cardiogenic shock due to right heart failure was intractable and despite maximal inotropic assistance and mechanical circulatory support (via ECMO), we could not stabilize the patient who subsequently passed away in severe right heart failure and cardiogenic shock.

Conclusion
Through this case report, we describe a very rare entity of right heart failure. Symptoms such as dyspnoea, syncope and haemoptysis in young patients should be immediately evaluated and in case of pulmonary hypertension patients should be referred to a heart centre for assessment of cardiac and pulmonary function in order to establish a focused diagnostic algorithm and define therapeutic goals.

P04-05

Impact Of Treatment Strategies And Hemodynamics On Short-Term Renal Outcome In Heart Transplant Patients

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Introduction
Renal failure is a common finding in patients with end stage heart failure and an entity with relevant impact on outcome in patients after orthotropic heart transplantation (OHT). We investigated the impact of baseline renal function, hemodynamics and diuretic treatment strategy on short-term renal outcome.

Methods
We collected date of 42 OHT recipients being transplanted between 2020 and 2021 with focus on renal function and renal outcome. Clinical characteristics including hemodynamic data and diuretic regimen were assessed. We performed regression analyses to identify predictors of short-term renal outcome defined as a change of renal function after seven days and one month.

Results
Of 42 OHT recipients with a median age of 54 (IQR 8), functional parameters showed ejection fraction of 21% (IQR 8), TAPSE of 13 mm (IQR 4) and Cardiac index of 1.8 L/min/m^2 (IQR 0.3). Right heart failure was present 16 patients (38 %) pre OHT. 13 patients (33 %) were supported mechanically and 22 patients with inotropes. Median pre-operative Creatinine was 1.72 mg/dL (IQR 0.80). On day 10, median Creatinine showed a maximum of 2.90 mg/dL (IQR 1.51) but stabilized on day 30 with 2.25 mg/dL (IQR 1.23). Higher baseline creatinine (p = 0.002) and higher CVP (p = 0.025) were associated with higher grade of renal failure one month after OHT.

We further found an association between right heart failure and stage II/III renal failure one month after OHT (p = 0.037, OR 5.7, 95% CI 1.3-25.9). Pre-operative hemodynamic standard parameters and diuretic drug management had no impact on renal outcome.

Conclusion
In our study, high baseline creatinine and high CVD on the first day after OHT were associated with a more severe decrease of renal function after OHT pointing out the importance of an optimized volume and fluid management in OHT candidates.

Further studies are needed to determine the optimal treatment regime for this topic with high impact on severity of chronic renal failure and survival after OHT.

P04-06

Rareisnot Rare Butspecial

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Introduction

Rare diseases, affecting 40/100,000 people [1], can lead to heart failure (HF) and need for heart transplantation (HTx) [2], [3], [4], [5].

Methods

We analysed the outcomes of patients (pts) that underwent HTx between 1991 and 2023 at the Leipzig Heart Center.

Results

In our cohort we found 63/584 pts with HTx by rare diseases: 15 pts had specific and rare cardiomyopathies (6 giant cell myocarditis and Loeffler endocarditis, 4 alcohol and drug abuse, 4 chemotherapy, 1 peripartum cardiomyopathy). 9 had left ventricular assist device (LVAD) support, 7 catecholamine (CA), 13/15 received HTx in HU status. (5 LVAD infection, 5 decompensated cardiac failure (DHF), 1 LVAD system defect, 1 LVAD thrombose, 1 arrhythmias). 6 died in follow up (f/u) with median (MD) 314,5 days (ds). 9 are in still in f/u MD 2082 ds.

8 pts had genetic hypertrophy cardiomyopathy, 7/8 got HTx as HU by DHF, 2 had LVAD, 7 CA, 2 died in f/u (MD 966 ds). 6 are in f/u for MD 1380,5 ds.

2 pts had Morbus Fabry and 1 glycogen storage disease, 3/3 got HTx as HU, 2 by DHF, 1 by arrhythmias, 3 had CA, 0 had LVAD, 1 had extracorporeal membrane oxygenation (ECMO). 1 died in 131 day f/u, 2 are in f/u (MD 1208 ds).

6 pts had genetic myopathy, 5/6 got HTx as HU by DHF, 1 had ECMO and LVAD, 4 CA, 1 died in 2062 ds of f/u, 5 are in f/u (MD 4428 ds).

3 pts had restrictive cardiomyopathy, 0 was HU, 0 had LVAD or CA. 2 died in f/u in MD 1928 ds). 1 is in f/u for 1612 ds.

3 pts had cardiac sarcoidosis, 2/3 had HTx as HU by DHF and had CA, 1 had ECMO, 1 LVAD, 2 died in f/u (MD 2611 ds). 1 is in f/u 3485 ds.

8 pts had arrhythmogenic right ventricular dysplasia, 8/8 got HTx as HU by DHF, 1 had LVAD and 3 CA. 4 died in f/u (MD 189,0 ds), 4 are in f/u (MD 4737 ds).

5 pts had non compaction cardiomyopathy, 4/5 got HTx as HU by DHF, 3 had LVAD and 3 CA. 1 died in f/u by 37 ds, 4 are in f/u (MD 2858 ds).

12 pts had congenital heart disease, 10 got HTx as HU, 6 by DHF, 1 by arrhythmias, 2 by LVAD infection, 1 by endocarditis, 4 had LVAD, 1 ECMO, 5 CA, 4 died in f/u (MD 2976,5 ds), 8 are in f/u (MD 2507 ds).

Conclusion

In our cohort rare disease showed a progressed disease stadium at time of transplant. Individual conditions have to be addressed to achieve successful HTx.

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P04-07

A High-Throughput Drug Discovery Pipeline To Optimize Kidney Normothermic Machine Perfusion

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Introduction
Kidney transplantation is the preferred therapy for end-stage kidney disease. The shortage of available organs presents a major obstacle in providing this treatment to all patients. Normothermic machine perfusion (NMP), a novel preservation technique, has the potential to enhance the number of transplantable kidneys. Despite its promise, there is limited knowledge regarding the cellular effects and potential pharmacological interventions during machine perfusion. While rodent models of NMP can be employed to explore molecular responses, they are technically complex, time-consuming, and limited in their capacity for large-scale replication.

Methods
To overcome this limitation, we developed a 3D-printed, high throughput ex-vivo mouse kidney slice incubator (KSI) that closely mimics mouse kidney NMP conditions. Using KSI, we tested the efficacy of five different pharmacological interventions. Promising drug candidates were subsequently applied in our mouse kidney NMP model. Tissue viability was assessed through immunoblotting, quantitative polymerase chain reaction (qPCR), and morphological analysis.

Results
The KSI model significantly reduced experimental time and increased sample throughput (theoretical: 54 incubations with n = 500/day). It effectively replicated cellular responses observed during NMP, particularly ER stress. Using the KSI, we evaluated five pharmacological interventions targeting ER stress based on existing literature. Four interventions proved ineffective and were therefore excluded. However, one intervention, β-Nicotinamide-adenine-dinucleotide (NADH), exhibited significant amelioration of ER stress during KSI. Subsequent testing of NADH in the mouse kidney NMP model replicated the positive effects on alleviating ER stress.

Conclusion
The KSI model represents a novel and highly efficient method for studying the targeting of molecular stress responses before conducting complex and time-consuming mouse kidney NMP experiments. The addition of NADH to the perfusion buffer showed promise in ameliorating ER stress. Further investigation into the use of NADH during clinical kidney NMP seems warranted.

P04-08

Introduction Of Normothermic Machine Perfusion Into Routine Clinical Practice – First Experiences From A Medium Volume German Transplant Centre

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Introduction
The most exciting development in liver transplantation (LT) of the past decade is continuous mechanical perfusion of donor organs. In times of organ shortage, normothermic machine perfusion (NMP) could possibly increase the use of marginal organs. NMP mimics physiologic liver perfusion using an oxygenated red blood

cell-based solution at 37.5°C. Putative effects include abrogation of preservation injury and ex vivo viability testing of high-risk donor allografts.

Methods
We included the first 12 LT organs from extended criteria donors between 01.01.2021 and 01.04.2023 at the University Hospital of Bonn subjected to NMP (Organox, Metra). During MP, we measured lactate level in the perfusate at several subsequent time-points. Standard postoperative values for transaminases, bilirubin and coagulation values were evaluated. We analysed postoperative complications (Clavien/Dindo (CD)) with a special focus to arterial and bile duct problems.

Results
NMP started after a median (range) cold storage period of 436 (402-511) minutes, for a time of MP of 334 (318-405) minutes. The median peak lactate level on pump during MP was 8 mmol/L, the median last lactate before LT was 2.07 mmol/L. The peak Bilirubin within the first 30 days was 6.4 mg/dL and the Bilirubin at day 5 was 4.7 mg/dL. The peak of ALT and AST were 841 and 1233 U/l, the ALT and AST levels at day 5 were 267 and 94 U/l. The median Quick at day 5 was 68%. The 30 days mortality rate was 0%. One liver developed a primary non-function. Major complications (CD≥ 3b) within 30 days after LT were seen in 7 patients. Biliary complications occurred in 3, and arterial complications in 3 patients.

Conclusion
NMP is safe and feasible even in a medium volume liver transplant centre. We did not experience any graft loss on pump due to surgical or mechanical complications. During every perfusion, the lactate level dropped adequately as a putative indicator of viability in high-risk grafts. Owing to the paucity of data, we were unable to establish a direct correlation between NMP and biliary/arterial complications in our recipients. Future studies are warranted to investigate possible associations.

P04-09

Genetic Engineering Of Limbs During Ex-Vivo Machine Perfusion

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Introduction
Ex vivo organ perfusion has the potential to mitigate ischemic-reperfusion injury (IRI), prolong preservation time, or even rescue organ function. It also provides a powerful delivery route for gene therapeutic agents such as lentiviral vectors (LV), increasing transduction efficiencies, organ specificity and safety. Genetic engineering of allografts towards reduction of IRI or graft immunogenicity may become potent tools to support graft survival. In this study, we aimed at developing a modular platform that allows genetic modification of vascularized composite allografts (VCA).

Methods
Rat limbs were perfused *ex vivo* under subnormothermic conditions for 4h with oxygenated perfusion solution and LV encoding a secreted nanoluciferase. Transduction efficiencies of the different limb tissues were determined by measuring the luminescence activity (Relative Luminescence Units, RLU) in tissue culture supernatants. Tissue integrity was investigated by histological analyses, quantification of lactate dehydrogenase (LDH) and myoglobin.

Results
Genetic modification was detected in all vascular, muscular, and dermal tissues 12 days after perfusion. Skin follicular and interfollicular keratinocytes as well as endothelial cells showed stable transgene expression. Compared to non-transduced negative control tissues (NCT), bioluminescence was detectable at high levels in artery tissue of $7.1\times10^5\pm6.0\times10^5$ RLU (NCT:

$4.5\times10^{1}\pm1.8\times10^{1}$) and in skin tissues of $9.1\times10^{5}\pm10.2\times10^{5}$ RLU (NCT: $0.8\times10^{2}\pm0.2\times10^{2}$). In the extensor digitorum longus and plantaris muscles bioluminescence values of $1.6\times10^{6}\pm1.4\times10^{6}$ RLU were detected. Levels of injury markers such as lactate, myoglobin, and LDH, as well as histological analyses showed that *ex-vivo* genetic engineering did not cause any tissue damage. Accordingly, limb cytokine secretion signatures were not significantly affected.

Conclusion

These data demonstrate that permanent genetic modification during ex vivo limb perfusion is efficiently possible. This platform holds the potential to evolve into a robust method to overcome the unresolved VCA rejection problem by reducing their immunogenicity and to take VCA transplantation to a next level.

P04-10

A Murine Model Of Hypothermic And Normothermic Kidney Machine Perfusion As A Platform For Insights Into The Allograft

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Introduction

Machine perfusion (MP) has made its way into the clinical practice for organ preservation. The importance of MP is growing as the regenerative potential can help meet rising organ demands by reconditioning organs retrieved from extended criteria donors (ECD). Currently, efforts are made to improve kidney preservation and reconditioning strategies by validating hypothermic MP (HMP) and normothermic MP (NMP) protocols, tested mostly by using expensive and labor-intensive large animal models with low animal numbers.

Methods

We established a murine kidney MP model allowing both HMP and NMP of murine kidneys with subsequent analysis of the organ as well as perfusate at comparatively low effort and costs to study the effects of MP on renal integrity and immune composition.

Results

Murine kidneys were perfused in a pressure-controlled manner at 80 mmHg. The perfusate was oxygenated with Carbogen (95% O2, 5% CO2) to a level of > 600 hPa. Using a cell-free perfusate, we were able to produce stable HMP perfusions for up to 2 hours. All grafts (n=10/10) remained viable to the end of the HMP period, showing a stable vascular resistance of 30 ± 10 mmHg/ml/min and a flow rate of 3 ± 1 ml/min. NMP was conducted using a perfusate substituted with human red blood cells allowing perfusion for 1 hour with a stable vascular resistance of 35 ± 10 mmHg/ml/min and a flow rate of 2.5 ± 1 ml/min. During NMP, all kidneys (n=10/10) were metabolically active and produced urine. Measurement of tissue injury markers including lactate dehydrogenase and aspartate transferase in venous perfusate of MP kidneys did not show a significant increase over time. We were able to phenotype extravasating lymphocytes and endothelial cells in the perfusate using flow cytometry. After MP, grafts were used for various analysis methods e.g. qPCR or confocal microscopy to evaluate the impact of MP on renal integrity.

Conclusion

In summary, we are able to conduct stable HMP and NMP using murine kidneys with subsequent analysis of the perfusate, perfusate cells & kidney graft in ways comparable to current trials using pig organs or discarded human organs. This model is superior to large animal models by allowing the comprehensive analysis of MP protocols on renal integrity. Additionally, it allows the testing of therapeutics for organ regeneration as well as the possibility for subsequent renal transplantation.

Poster Session 05: Infectiology / Immunology

P05-02

Follow-Up Of Serotype-Specific Antibodies After Sequential Vaccination With PCV13 And PPSV23 In Kidney Transplant Recipients

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Introduction

Vaccination against *Streptococcus pneumoniae* is recommended in transplant recipients to reduce the morbidity and mortality from invasive pneumococcal disease. Previous studies indicate that transplant recipients can produce specific antibodies after vaccination with the 13-valent pneumococcal conjugate vaccine Prevenar 13 (PCV13) [1] or the pneumococcal polysaccharide vaccine Pneumovax 23 (PPSV23) [2]. National guidelines recommend sequential vaccination with PCV13 followed by PPSV23 in kidney transplant patients. However, there are currently no data on the serological response in kidney transplant recipients, who received a sequential vaccination with PCV13 and PPSV23.

Methods

In the current study, we sequentially vaccinated 46 kidney transplant recipients with PCV13 and PPSV23 and determined serotype-specific and global anti-pneumococcal antibody responses in the year following vaccination.

Results

Serotype-specific and global anti-pneumococcal antibody concentrations were significantly higher compared to baseline. We observed that serotype-specific antibody responses varied by serotype (between 2.2- and 2.9-fold increase after 12 months). The strongest responses after 12 months were detected against the serotypes 9N (2.9-fold increase) and 14 (2.8-fold increase). Global antibody responses also varied with respect to immunoglobulin class. IgG2 revealed the highest increase (2.7-fold), IgM the lowest (1.7-fold). Sequential vaccination with both vaccines achieved higher antibody levels in comparison with a historical cohort studied at our institute, that was vaccinated with PCV13 alone. During the 12-months follow-up period, none of the patients developed pneumococcal-associated pneumonia or vaccination-related allograft rejection.

Conclusion

In conclusion, we strongly recommend sequential vaccination over single immunization in kidney transplant recipients.

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P05-03

Spot On Herpesviruses – T Cell Monitoring Of Our Livelong Companions

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Introduction

The interaction between the host immune system and the herpesviruses is critical as they can establish a life-long persistence with the risk of reactivation causing from mild to severe diseases with possible fatal outcome. The 8 human pathogenic types have infection rates of up to 95% worldwide, depending on the genus, and cause partly life-threatening diseases with a focus in transplantation medicine, which make these viruses a serious healthcare burden. Characteristically, severe disease and mortality in immunocompetent individuals caused by α- and γ-herpesviruses are rare. The more or less peaceful coexistence of the herpesvirus and its host can change, however, under several circumstances such as immunosuppression.

Methods

The EliSpot assay is able to detect one pathogen-specific T cell in 2x10e5 PBMCs. Since other diagnostic methods are not able to detect functional immune cells, it is in special settings required to monitor the immune status for the detection of an arising immunoreaction against latently viruses, especially in the field of transplantation.

Results

The established EliSpots with antigens against EBV, CMV and also HSV 1&2 have been extended to include the detection of specific T cells against VZV, HHV 6, 7 and 8. The assay design is based on the secretion of Interferon-gamma (IFN-y) in an enzymatic EliSpot system, which is easy, fast and robust to handle even in high-throughput routine diagnostics. The antigen preparations allow the discrimination of lytic (active) immune responses and latent t cell responses, which is an outstanding advantage compared to other diagnostic tests. Dormant and asymptomatic active infections can be distinguished and furthermore, with the complete herpesvirus antigen panel, infections out of the main focus (HHV 6-8) can be diagnosed and monitored. As T cell reactions are dynamic and fast, the EliSpot enables physicians a nearly real-time monitoring of immune reactions, which is important in transplantation and/or oncologic settings.

Conclusion

The claim of more and better individualized immuno-monitoring is perfectly fulfilled with the EliSpot, as it is a useful tool to track the dynamic changes in the immune response and status of the patients.

P05-04

Infection Status Of The DZIF-Renal-Transplant Cohort And A Cross-National Comparison To Other Transplant Cohort Studies

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Introduction

Infectious diseases are a major challenge in the post-transplant setting. Some may constitute a general burden in renal transplant recipients, others might be more influenced by local determinants. We aimed to compare

the current infection status of a renal transplant cohort in Germany to 5 foreign renal transplant cohorts.

Methods

In this prospective multicenter study of the German Center of Infectious Diseases (DZIF), all infections of the first year after renal transplantation were collected. Incidences and microbial aetiology were compared to 5 foreign renal transplant cohorts, including Swiss (Swiss Transplant Cohort Study (STCS), n=1612), Argentina (n=375), Iran (n=193, n=133) and Greece (n=142) (2002-2019). Standard immunosuppression consisted of CNI, MPA and steroids. Anti-infective protocols included prophylaxis for Pneumocystis jirovecii and Cytomegalovirus (CMV).

Results

Comparable to other European cohorts, recipient age was 51±14 years in DZIF, but older compared to Iran (34± 12). In all cohorts most infections were caused by bacteria, followed by viruses and fungi (means: 61%/25%/5%, DZIF: 67%/29%/5%). Gramnegative enterobacteria (mostly E.coli) were the main urinary tract pathogens. Blood stream infections occurred in 1 - 7% (DZIF: 4%). Whereas viral opportunists were the most common viruses (e.g. CMV), bacterial opportunists were reported rarely. BK viremia/nephropathy was only reported in DZIF (11%/2%) and STCS (16%/6%). Candida albicans was the most common fungus (DZIF:41%). Pneumocystis jirovecii and Aspergillus fumigatus were scare and mainly reported in DZIF and STCS (14%/14% and 9%/10%). Microbial aetiology in DZIF was most in line with the STCS-data. Relevant numbers of parasite infections were only observed in distinct latitudes (Argentina, Iran).

Conclusion

Irrespective of the geographic area, the majority of renal transplant recipients suffer at least one infection during the first year - mostly of bacterial origin. E.coli is a leading urinary tract pathogen, CMV represents a major viral opportunist and Candida albicans is the predominating fungus. The isolation of other fungi and parasites seems to depend more strongly on the countries' endemic profile.

P05-05

Urinary Tract Infection In Renal Transplant Recipients – Results Of The DZIF (Deutsches Zentrum Für Infektionsforschung) Transplant Cohort

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Introduction

Renal transplant recipients are predisposed to urinary tract infections (UTI). Epidemiology and pathogen susceptibility may vary widely depending on recipients' characteristics and the time elapsed since transplantation. Precise data of a large multi-center transplant cohort in Germany are lacking.

Methods

This prospective multi-center study is based on the Transplant Cohort of the German Center for Infectious Diseases (DZIF) and includes all adult renal transplant recipients enrolled from 04/2014 to 11/2019 (n=804). All UTI episodes (defined as the presence of suggestive symptoms and a positive urine culture) of the first posttransplant year were evaluated. Trimethoprim-sulfamethoxazole was provided for 6 months.

Results
UTI were responsible for 42.4% (412/972) of all infections, affecting 30.3% (244/804) of our cohort. 55.0% of all episodes occurred within the first 3 months, 75.1% within the prophylaxis period. The median time to the first UTI was 42 days (IQR=14-101). More than a quarter of UTI patients were suffering recurrent UTI (26.6%) or were affected by resistant strains (25.8%). The most common pathogens were E.coli (23.4%), Enterococcus spp. (23.0%, 46.6% VRE), Klebsiella spp. (15.6%). Enterococcus and Klebsiella spp. were significantly more prevalent in recipients with recurrent UTI. Enterococcus was predominating during the first month and between month 6 and 9 - E.coli during the rest of the first year. In multivariate analysis recipient age and the number of postoperative in-patient days were associated with Enterococcus-, Klebsiella spp. and Pseudomonas aeruginosa isolations, but also with bacterial resistance. Female gender was associated with a higher incidence of E.coli (17.4% vs. 10.9%, p=0.009), whereas males mere more prone to Pseudomonas aeruginosa (6.6% vs. 2.2%, p=0.007).

Conclusion
30% of renal transplant recipients suffer at least one UTI during the first posttransplant year. Sufficient prophylaxis needs to consider the current aetiology but also varying pathogen susceptibilities amongst the recipients. Special attention should be paid to aged recipients with a prolonged hospital stay and to pathogens associated with recurrent UTI episodes.

P05-06

Cytomegalovirus Infections In The Transplant Cohort Of The German Center Of Infectious Diseases (DZIF)

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Introduction
Cytomegalovirus (CMV) infections are the most common infections after renal transplantation. CMV incidence-rates, prophylaxis strategies and their side effects have not been comprehensively studied in a German transplant cohort.

Methods
In this prospective multicenter study of the German Center of Infectious Diseases (DZIF) CMV infections observed during first year after renal transplantation and adherence to KDIGO guidelines were evaluated. Our cohort comprised all adult renal transplant recipients included in the DZIF cohort by 5 large German transplant centers from 04/2014 to 02/2022.

Results
1035 recipients (64.6% male, age 51±14y) were enrolled. Nearly all (99.7%) received CNI, MPA and steroids. CMV replication occurred in 14.3% [12.3;16.5] of all recipients - in 74.5% withinand in 25.5% after prophylaxis. Multivariate analysis revealed deceased donation, D+/R- and T-cell-mediated rejection as risk factors. At baseline, CMV prophylaxis was prescribed to 76.3% of recipients for at least 3 months. CMV-prophylaxis protocols of 4 centers were similar to KDIGO-guidelines (617 (59.6%) patients). One center recommended a 3-month prophylaxis for D+/R- group and no prophylaxis for D-/R+ group. Cumulative CMV-incidence of this center was 18.3% [14.9;22.5] compared to 11.6% [9.3;14.4] the other centers (p=0.003). Clinical practice discrepancy was observed in at least 26.3% of patients, primarily in D-/R- (34.6% with prophylaxis) and D-/R+ group (37.3% without prophylaxis). Leucopenia was observed in 15.6% in patients with prophylaxis and in 5.4% without prophylaxis (p=0.003). Post-prophylaxis-viremia occurred in 8.4% [6.8;10.3] of the total cohort, in 34.0% [24.7;46.7] of D+/R- recipients with a 3-month- and in 7.3% [3.4;15.8] with a 6-month-prophylaxis (p<0.001).

Conclusion
Renal allograft recipients in Germany experience a high burden of CMV infections despite of existing prophylaxis guidelines. Non-adherence is a strong determinate of

CMV replication, but prophylaxis also bears a risk for leukopenia. Prolonged CMV prophylaxis reduces the incidence of CMV - also in the post-prophylaxis time. Future studies should place a stronger focus on CMV prophylaxis strategies and its consequences.

P05-07

Long-Term Immune Dysregulation After Rituximab Induction In ABO Incompatible Living-Donor Renal Transplantation – Impact On Chronic BK Virus Infection

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Introduction

We previously described a key role of IL-10 in chronic BK virus infection after renal transplantation. As an increased frequency of BK viremia has been reported after ABOi renal transplantation, we analyzed clinically relevant immune parameters in a 5-year prospective renal transplant study.

Methods

Mononuclear cell subsets (peripheral blood; regional lymph nodes; protocol biopsies (n=58, 3 months; n=34, 1 year)), intracellular cytokine and in-vitro B cell responses were assessed up to 5 years posttransplant in 85 renal transplant recipients (living donation: n=25 ABOi (with rituximab induction) and n=30 ABOc; DD: n=30 ABOc).

Results

The incidence of BK viremia was significantly enhanced in rituximab versus non-rituximab treated patients (P=0.009, 1 year; P=0.029, 5 years). Whereas intracellular IL-10 production was not increased in ABOi patients, IL-10R expression on monocytes was enhanced at 3 months (P=0.009 vs. DD, P=0.037 vs. ABOc) and 5 years (P=0.015 vs. ABOc). In protocol biopsies we found rituximab-induced B cell depletion in ABOi patients at 3 months (P<0.001 vs. ABOi and DD), but comparable B cell counts and even enhanced counts of CD3+ T cells (P=0.041), CD68+ macrophages (P=0.021) and CD138+ plasma cells (P=0.033) at 1 year. After rituximab induction in ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years together with impaired B cell responses for 2 years (P=0.010, T-dependent; P=0.053, T-independent). T cell counts were lower in ABOi versus ABOc recipients up to 6 months (CD4+ T cells, 6 months P=0.046; CD8+ T cells, 3 months P=0.011). In regional lymph nodes of ABOi patients, we found a significant rituximab-induced downregulation of CD20+ B cells (P<0.0005), of naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation.

Conclusion

An increased frequency of BK viremia in rituximab-treated renal transplant recipients may be explained by increased IL-10R expression, downregulated CD4+ and CD8+ T cell counts, a profoundly delayed B cell repopulation together with compromised B cell responses and compromised antigen presentation due to B cell depletion in the graft and regional lymph nodes.

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P05-10

The DZIF Transplant Cohort

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Introduction
The DZIF Transplantation Cohort e.V. is a large multicenter prospective observational cohort of transplant recipients and donors, enabling extensive collection of medical data as well biological samples. Infections in transplant recipients have a major impact on the overall therapy success and clinical outcome. However, many issues regarding long-term consequences of infections are not well understood. The transplant cohort collects a wide range of medical data and biospecimens and makes them available upon request.

Methods
Collection of data and samples takes place in university hospitals and clinics in Hannover, Heidelberg, München and Tübingen at time of transplantation, after 3, 6, 9 and 12 months and then yearly thereafter; as well as in case of infection. The cohort enables studies to investigate correlations between infections and immune alterations with the development of transplant complications in a prospective manner. Biosamples are preserved in a quality conform to state-of-the art genomic and epigenomic technologies for future analyses. The distribution of data and samples to researchers is linked to a detailed review process by the cohort internal scientific steering committee and a pool of external international reviewers.

Results
Up to now, there are about 2.370 patients included in the data base and more than 44.300 biosamples collected, including PBMCs, RNA-stabilized blood, serum, urine, feces.

Conclusion
Worldwide there exist only few and relatively small prospective cohort studies on transplant patients with a focus on infectious disease. Therefore, the DZIF Tx Cohort will contribute significantly to a more careful epidemiological and experimental analysis of the impact of infections on transplant function and survival by using standardized protocols for the collection of multiple biosamples and patient data at defined time points before and after transplantation.

P05-11

Mycotic Thrombosis Of A TIPS In A Liver Retransplant Candidate

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Introduction
Infection of a transjugular intrahepatic portosystemic shunt (TIPS) stent is a rare and serious complication on the liver waiting list. Most commonly it occurs during TIPS creation or revision. Patients typically present recurrent infections due to shunt occlusion or vegetation.

Methods

We report on a single case of a 51-year old liver recipient who presented with recurrent infection caused by candida albicans awaiting retransplantation. First liver transplantation (LT) was performed in 2019 due to virus related liver cirrhosis and relisting for retransplantation on 31.05.2022 due to ischemic type biliary lesions (ITBL). We focused on the subsequent mycotic TIPS thrombosis caused by the candidemia.

Results

In July 2022, a portal vein thrombosis was found as the reason for recurrent ascites. Therefore, a TIPS was implanted on 25.10.2022. Two weeks later, fever occurred and blood cultures were positive for candida albicans. Antimycotic therapy was initiated with Anidulafungin and switched to Voriconazol in November and Echinocandin in December 2022. After negative blood cultures in the meanwhile the second detection of candidemia occurred on 15.02.2023. Also, ascites was increasing and an ultrasound showed an occlusion of the TIPS, which seemed to be linked to the candidemia. Therefore, a TIPS-revision was performed on 17.02.2023. After intensive screening, an uveitis of the left eye was a likely source of candidiasis. However, recurrent candidemia, following portal vein occlusion after TIPS-implantation seemed to be linked as a mycotic TIPS-infection that could be cured by retransplantation. A non-standard exception was granted by Eurotransplant on 31.05.2023. The histological results of the explanted liver confirmed a massive mycotic TIPS thrombosis with colonization of the explanted liver.

Conclusion

Mycotic thrombosis of a TIPS prior to liver transplantation is rare complication that can be cured by liver transplantation. However, the proof of this diagnosis is difficult and might be found earliest in the explanted liver by the pathologist.

P05-12

HLA Typing With Nanopores: Third Generation Typing (TGS), The New Era Of HLA Definition And The Benefit For Virtual Crossmatching

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Introduction

Since January 2023, the virtual crossmatch is implemented in the allocation procedureby Eurotransplant, to minimize the risk of rejection and graft loss post transplantation. The virtual crossmatch based on the definition of unacceptable antigens that may be targeted by antibodies against the organ donor. In this case the antibodies can cause positive crossmatches, due to binding to specific epitopes. The latter can only be determined by extended HLA typing at a high-resolution level in other words Aa high-resolution HLA typing is necessary for transcribing HLA alleles into epitopes. Epitopes are specific structures on proteins that are recognized by the immune system, here the humoral part. If the immune system of the recipient recognizes epitopes on the donor organ as non-self, rejection or graft loss might be the consequence.

Methods

Here, we show the validation results of high-resolution HLA typing by the Oxford Nanopore technology, which allows definition of the alleles for 11 loci in 4-5 hrs. A DNA fragment enters a nanopore and each DNA base disrupts the electrical field with a specific signature and can be used as a single molecule detector. The electric signal is converted into a DNA sequence with a fastq output format, which can be analyzed by special software.

Results

We analyzed, so far, about 50 DNA samples with this TGS and compared them with high-resolution previous results. We used the NanoTyper software and the IMGT/HLA database 3.51.0. The results of all tested samples are consistent with the previous NGS results and conformed the EFI standards. In addition, we observed one possible new class I and four class II alleles which must be confirmed.

Conclusion

This new technology based on nanopores is reliable for high resolution typing. It is cost-effective and shows no ambiguities due to longer read length. It is easy to learn and fast for a single sample (4-5 hrs.) This brings a great advantage not only for patients but especially for post-mortem donors in duty hours. Recipients and donors, postmortem or living, can be typed at high resolution allowing the use of an epitope matching algorithm optimizing and improving the virtual crossmatch and the transplantation outcome.

P05-13

Epigenetic Immune Cell Characterization In Urine Early After Kidney Transplantation Allows Prediction Of Long Term Kidney Function

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Introduction

The early immune response after kidney transplantation can lead to significant damages of the graft, which might impair its immediate and long-term function. Characterizing the immune cell subsets involved in the early detrimental or protective reactivity could lead to diagnostic improvements and new therapeutic interventions. Flow cytometry can be used for this purpose, but has significant challenges in terms of sample handling, reproducibility and quantity of subsets that can be studied.

Methods

We made use of the epigenetic immune phenotyping platform of Epiontis ID to characterize and quantify frozen urine sample pellets of 39 kidney transplant patients collected within three months after transplantation. Via epigenetic real-time qPCR we quantified 12 immune cell subsets: CD3, CD4, and CD8+ T cells, memory CD4+ and regulatory T cells, IL17+, Granulysin+, CXCR3+, and CCR6+ cells, as well as NK cells, Neutrophils, and B cells. To normalize for gender biases leading to different numbers of cells found in the urine, we analyzed ratios of the relative immune cell counts. GFR was monitored early after transplantation and during the first post-transplant year.

Results

38% of patients developed a delayed graft function after transplantation. The CD4/CD8 T cell ratio was elevated in patients with DGF during the first week after transplantation, but these patients had relatively fewer memory CD4+ T cells in urine. As expected, patients with DGF had a significantly lower GFR also one year after transplantation as compared to the non-DGF cohort. Interestingly, the NK cell/neutrophil ratio in the urine within the first month after kidney transplantation was a better discriminator between impaired and good long-term transplant function than DGF status.

Conclusion

We demonstrate the feasibility of epigenetic immunophenotyping of urine-derived immune cells after kidney transplantation. This allows the identification of early markers for the risk of early and long-term kidney function impairment. Thus, this test could deepen our understanding of the immune processes in the kidney allograft after transplantation and potentially allow for an early risk stratification and treatment adaptation.

P05-14

CXCR4 Blockade Reduces The Severity Of Murine Heart Allograft Rejection By Plasmacytoid Dendritic Cell-Mediated Immune Regulation

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Introduction

Allograft-specific regulatory T cells (T_{reg} cells) are crucial for long-term graft acceptance after transplantation. Although adoptive T_{reg} cell transfer has been proposed, major challenges include graft-specificity and stability. Thus, there is an unmet need for the direct induction of graft-specific T_{reg} cells. We hypothesized a synergism of the immunotolerogenic effects of rapamycin (mTOR inhibition) and plerixafor (CXCR4 antagonist) for T_{reg} cell induction.

Methods

BALB/c (allogeneic) or C57BL/6J (syngeneic) mice served as heart donors and C57BL/6J as transplant recipients. Animal experiments adhered to EU directive 2010/63/EU and were approved (#G1071/09). Heterotopic intra-abdominal heart transplantation (HTX) was performed as previously described (1). Allograft function was evaluated daily by palpation. C57BL/6J recipients received injections with plerixafor (1 or 5 mg/kg s.c.) and/or rapamycin (0.4 mg/kg i.p.) two days before, immediately after HTX and every other day for 14 days. The subclinical dosage of rapamycin allowed to early distinguish differences in allograft survival.

Results

The combined treatment consisting of Plerixafor and Rapamycin lead to a longer prolongation of allograft survival compared to rapamycin-only ($p<0.001$). Median allograft survival time in recipients from the non-treatment, plerixafor (P1 and P5 mg/kg), rapamycin and combined treatment group P1R or P5R were 8, 10, 10, 44, 49 and 78 days, respectively. Hearts of the respective syngeneic controls survived the whole observation period of 100 days. Moreover, fibrosis and myocyte lesions were significantly reduced in the combined treatment group when compared to sole Rapamycin-treatment. Although less $CD3^+$ T cell infiltrated, higher T_{reg} cell numbers were observed. These findings were accompanied by a plerixafor-dependent plasmacytoid dendritic cell-mobilization as in vivo pDC-depletion abrogated the plerixafor-mediated increase in T_{reg} cell numbers and led to a reduced allograft survival.

Conclusion

Our pharmacological approach allowed to increase T_{reg} cell numbers due to pDC-mediated immune regulation. Therefore pDCs can be an attractive immunotherapeutic target in addition to plerixafor treatment.

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P05-15

Safety And Immunogenicity Of The mRNA-1273 Vaccine In Solid Organ Transplant Recipients

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Introduction
Immunosuppressed people are at high-risk for severe COVID-19. A 3-dose primary series with an updated mRNA COVID-19 vaccine is recommended; an additional updated vaccine dose may be indicated ≥2 months later. Clinical data evaluating mRNA-1273 in immunosuppressed populations are needed.

Methods
Study P304 is an open-label, phase 3b trial evaluating mRNA-1273 safety and immunogenicity in 137 adult kidney and 77 liver solid organ transplant recipients (SOTRs) and 20 healthy participants. In Part A, SOTRs received ≤3 doses of 100-µg mRNA-1273; healthy participants received 2 doses. In Part B, a 100-µg BD was offered ≥4 months from the last primary series dose. Neutralizing antibody (nAb) geometric mean concentrations (GMCs) vs ancestral SARS-CoV-2 Spike protein and binding Ab (bAb) GMCs vs ancestral SARS-CoV-2 and variants of interest were assessed.

Results
In baseline-SARS-CoV-2-negative SOTRs, mRNA-1273 elicited modest nAb responses 1-month post-dose 2. At 1-month post-dose 3, mRNA-1273 enhanced Ab responses; nAb in liver SOTRs (GMC, 1361.5; 95% CI, 668.4-2773.4) were comparable to post-dose 2 responses in healthy participants (1632.8; 970.3-2747.8) and to Study P301 participants (Day 57, 1111.0; 1043.8-1182.5). At 1-month post-BD, mRNA-1273 boosted nAb responses vs pre-BD regardless of primary series vaccine type. Post-BD (Day 29) enhancement vs post-dose 2 in liver SOTRs was ~3-fold (3946.0; 1944.5-8007.8) but lower than healthy participants (9943.5; 4609.9-21447.7) and P301 participants (8173.9; 7645.7-8738.4). Reduced Ab responses were observed in kidney vs liver SOTRs; most were on multiple immunosuppressants. Similar trends were observed for bAb, including against variants; bAb responses were lower against omicron vs other variants. mRNA-1273 was well-tolerated in SOTRs. Four vaccine-related SAEs in 3 SOTRs were reported by the investigator, which may have been related to pre-existing comorbidities. No vaccine-related biopsy-proven organ rejection or death was reported.

Conclusion
Three doses and a BD of mRNA-1273 (100-µg) had an acceptable safety profile and enhanced immune responses in SOTRs. SOTRs on multiple immunosuppressants, particularly kidney SOTRs, had reduced Ab responses.

Poster Session 06: Kidney Transplantation

P06-01

The Molecular Microscope Diagnostics System (MMDx) May Have The Potential To Differentiate Molecular T-Cell Mediated Rejection Among Kidney Transplant Recipients With Chronic-Active T-Cell Mediated Rejection

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Introduction
Treatment of chronic-active T-cell mediated rejection (caTCMR) lacks consensus, causing many different therapeutic approaches. If changes in transcript patterns analyzed by the Molecular Microscope Diagnostic System (MMDx) may differentiate among these cases with caTCMR and offer additional diagnostic value needs to be evaluated.

Methods
In this single-center cohort of 326 indication kidney transplant biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 15 cases with caTCMR after the exclusion of overlapping pathologies such as BK nephropathy, pyelonephritis, and acute interstitial nephritis. 7 cases with combined acute TCMR and caTCMR were compared to 8 cases with caTCMR only.

Results
3 of 7 cases (43%) with combined acute TCMR and caTCMR, and 1 of 8 cases (13%) with caTCMR only showed pure molecular TCMR. In addition, 3 of 7 cases (43%) with combined acute TCMR and caTCMR, and 4 of 8 cases (50%) with caTCMR only showed mixed molecular ABMR/TCMR with histologic ABMR in 5 of 7 cases (71%). Among 3 of 8 cases (38%) with caTCMR only but no molecular rejection, 2 cases showed an all ABMR rejection phenotype score (sum of R4, R5, and R6) $\geq$0.20, and 1 case showed a TCMR phenotype score (R2) $\geq$0.10.

Conclusion
The MMDx may have the potential to differentiate histologic caTCMR into molecular TCMR, molecular ABMR/TCMR, or no molecular rejection. Whether the observed minor molecular findings are attributable to undetected overlapping findings other than rejection, cortex/medulla sampling variations, or a suspected continuum of caTCMR needs to be studied.

P06-04

Multicenter Evaluation Of Complex Urinary Diversion For Renal Transplantation: Outcomes Of Creative Surgical Solutions

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Introduction
Complex urinary diversions for kidney transplantation (KT) are rarely necessary. Besides the ureteral anastomosis to an ileal conduit, many creative solutions exist. Standardization and teaching is extremely difficult, because of the small patient group.

Methods
The reasons and outcomes of complex urinary diversions after KT were retrospectively evaluated at eight German urologic transplant centers including a current follow-up.

Results
Of 39 patients with complex urinary diversion, 22 (56%) were male at a median BMI of 24.8 kg/m^2 (range 16.6; 36.2). The most common causes of terminal renal failure were vesicoureteral reflux (18%), spina bifida (16%), and glomerulonephritis (10%). Surgical urinary diversion had been performed in 28 (72%) patients before KT, at a median of 112 (range, 10; 545) months. The transplantation themselves were carried out between 1986 and 2019 at a median patient age of 42.5 years, in 33 (84%) cases as a postmortem donation. Urinary diversion was modified during KT in 13 (33%) patients. After transplantation, the ileal conduit was the most common form of incontinent urinary diversion in 26 (67%) patients, and a Mainz pouch I or bladder augmentation represented the most common continent urinary diversion in 3 (7.6%) patients each. Intraoperative complications occurred in only one case and postoperatively in 6 (15%) patients. At a median follow-up of 92 (range 6; 431) months, the median serum creatinine 1 year post KT was 1.4mg/dL (0.46; 2.92), at 5 years 1.6mg/dL (0.7; 10.1). At a median graft survival of 155 (95%CI 111.4; 198.6) months, graft failure occurred in 13 (33.3%) patients, mainly due to 7 (53.9%) rejections.

Conclusion
The 5-year graft function of kidneys with complex urinary diversions appears to be stable and comparable to transplants with regular urinary diversions. Therefore, complex urinary diversion should always be considered as a surgical option in special cases, even during transplantation, if necessary, and prior surgical experience in urological diversions appears to be very helpful.

P06-08

The Need For Better Lipid Management: A Single-Center Cross-Sectional Analysis On Current Lipid Control Status In Kidney Transplant Recipients

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Introduction
In kidney transplant recipients (KTRs), cardiovascular mortality remains the leading cause of death. Dyslipidemia, one of the major cardiovascular risk factors, occurs frequently after kidney transplantation. Despite lipid lowering therapy (LLT), insufficient lipid control in KTRs is common. Inclisiran, a novel small interfering RNA (siRNA) that inhibits the synthesis of PCSK9, has so far shown promising results as an additional therapeutic strategy in lowering LDL-cholesterol (LDL-C) levels. However, until today there is only very limited data on usage of inclisiran in KTRs. We analyzed the current lipid control status of

KTRs to evaluate the potential applicability of additional inclisiran therapy at our institution.

Methods

We conducted a single-center, cross-sectional analysis of KTRs who were followed up in our outpatient clinics in 2022 regarding patient characteristics, statin and/or ezetimibe therapy and LDL-C levels.

Results

In 2022, 1721 patients who received a kidney transplant between 2000 and 2022 were followed up in our outpatient clinics with an average time after kidney transplantation of 8.4 years (range 5 months-23 years). 1087 patients (63.2%) were male and 634 (36.8%) female. Median patient age was 57 years (range 19-86 years). Mean BMI±SD (kg/m^2) was 24.2±7.3 (24.6±6.7 in male and 23.5±8.2 in female patients respectively, p<0.001). 1682 KTRs (97.7%) were on LLT. LDL-C levels were measured from 1140 KTRs on LLT (67.8%). Mean LDL-C level±SD (mg/dl) was 105±36 (102±37 in male and 110±36 in female patients respectively, p<0.001). Despite being on LLT, 935 KTRs (82%) showed elevated LDL-C levels of >70mg/dl. In only 205 KTRs (18%) LDL-C levels were within the recommended target range of <70mg/dl for very high-risk patients according to the ESC/EAS guidelines.

Conclusion

Our institutional analysis showed sub-optimal LDL-C control in KTRs despite ongoing LLT. As cardiovascular disease remains the leading cause of mortality in KTRs, better lipid management is highly required to reduce cardiovascular risk. Additional implementation of inclisiran in KTRs could be a promising novel therapeutic strategy for improved lipid control and should be further examined in future studies.

P06-09

Optimization Of The Tacrolimus Concentration-To-Dose Ratio Cut-Off Value To Define Metabolism Groups

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Introduction

The tacrolimus (Tac) concentration to dose ratio (C/D ratio) has been described as a predictive marker for several outcome parameters after renal transplantation (RTx) [1,2]. Up to now, different C/D ratio cut-off values were used to discriminate fast Tac metabolizers (low C/D ratio) from slow metabolizers (high C/D ratio) [3,4]. We hypothesize that an optimal C/D ratio cut-off can be determined by the use of a statistical software with a high predictive value for kidney function development.

Methods

Data of 389 RTx patients was analyzed who received an initial immunosuppression with immediate-release tacrolimus (IR-Tac), mycophenolate, prednisolone, and an induction with basiliximab. The Tac C/D ratio (ng/mL*1/mg) of all patients was calculated 3 months after RTx and the maximally selected Wilcoxon statistic R Package was applied to determine the optimal C/D ratio cut-off value for renal function development in a 5-year follow-up.

Results

It was confirmed that fast Tac metabolizers developed an impaired renal function compared to slow metabolizers. An optimal C/D ratio cut-off was found to be 0.94 for the follow-up time points at 1, 2, 3 and 4 years and 0.95 at 5 years after RTx.

Conclusion

As fast Tac metabolism is associated with the development of an impaired renal function, it is essential to identify patients at risk early after RTx. In order to keep the application easy for clinical routine, we suggest to calculate the C/D ratio at month 3 with the cut-off value of 1.

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P06-10

Prolonged Cold Ischemia Time Is A Risk Factor For Delayed Graft Function And Increased Mortality In Kidney Transplant Recipients Within The Eurotransplant Senior Program

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Introduction

Confronted with an aging population of listed renal failure patients, the Eurotransplant Senior Program (ESP) not only reduces median waiting time by at least a year compared to standard allocation for patients ≥ 65 years (1), but was also found to double their life expectancy compared to remaining on dialysis (2). However, older organs have been found to have an increased susceptibility to prolonged cold ischemia time (CIT) (3, 4). Therefore, to minimize CIT, both kidneys of one donor are often allocated to the same transplantation center. This study examines the influence of CIT on delayed graft function (DGF) and long-term outcome by comparing the data of consecutively transplanted ESP patients receiving kidneys from the same donor.

Methods

This monocentric retrospective study with a mean follow-up of 5.7 years includes all 208 kidney transplantations (KTx) allocated via the ESP at the Freiburg Transplant Center from 1999 to 2019. We compare 74 pairs of kidneys transplanted consecutively into 2 ESP patients, defining them as "rank 1" and "rank 2 recipient". To quantify CIT, we divide our cohort into 3 groups: CIT 1 (0-480 min), CIT 2 (481-720 min) and CIT 3 (≥ 721 min).

We describe distribution of DGF, allograft survival and mortality according to CIT. To test for the association of CIT with DGF, we use a mixed logistic regression analysis.

Results

DGF was comparable for rank 1 and rank 2 recipients. However, solely regarding CIT, an extension over 720 min was associated with a 4.9-fold risk of DGF compared to a CIT under 480 min (adjusted OR 4.93; 95% CI: 1.34 – 18.19, p = 0.017). Death-censored allograft survival was not influenced by the length of cold storage. CIT over 720 min, though, increased mortality by 3.2-fold (adjusted HR 3.19, 95% CI: 1.44 – 7.49, p = 0.005).

Conclusion

Consecutive KTx of a pair of kidneys allocated via the ESP to one transplantation center is not related to a worse outcome for the second recipient when transplanted within 720 min. However, a CIT exceeding 720 min quintuples the risk for DGF and is an independent predictor of increased mortality after KTx.

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P06-12

Optimizing Surgical Approaches In Transplant Nephrectomy. A Comparative Study Of Timing And Techniques

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Introduction

Transplant nephrectomy (TN) has historically been associated with high morbidity and mortality rates. Our objective is to share our own experience and compare indications and surgical outcomes between early and late TN and intracapsular (ICAN) and extracapsular allograft nephrectomy (ECAN) techniques.

Methods

Our study included all 69 TN procedures performed between January 2010 and February 2021. Of these, 17 TN procedures were performed within the first 60 days after transplantation (referred to as 'early'), while the remaining 52 procedures were performed later ('late'). Within the late allograft nephrectomy (AN) group, we compared the outcomes of intracapsular (ICAN) and extracapsular (ECAN) techniques. We conducted a statistical analysis using the chi-square test and the 2-sample Student´s t-test.

Results

The primary indication for early TN was surgical transplant complications (94.1%), with 58.8% of these cases requiring emergency surgery. Morbidity (major complications) occurred in 47.1% of cases, and mortality was 5.9%. In contrast, graft intolerance syndrome was the leading indication for late TN (76.9%), with elective surgery performed in 88.5% of cases. Morbidity (major

complications) occurred in 11.5% of cases, and mortality was 3.8%. Within the late TN group, 82.7% of cases were treated with ICAN and 17.3% with ECAN. Blood transfusion was required during surgery in 17.3% of cases, with no significant difference between the groups. Multivariate logistic regression analysis revealed that the timing of surgery was the only statistically significant predictor of complication occurrence.

Conclusion

Our data suggest that TN can be performed with relatively low morbidity. However, early TN remains the only independent risk factor for developing adverse outcomes.

P06-15

Interactions Between TTV, EBV, CMV And BKV And Their Impact On The Post-Transplant Graft Function In Kidney Transplant Recipient

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Introduction

Reactivation of latent viruses such as Torque Teno Virus(TTV),BK virus (BKV), Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) are common after kidney transplantation. They are known to be associated with increased morbidity and mortality. Although CMV might be a risk factor of other infections, the effects of CMV/BKV/TTV/EBV interactions and of combined reactivations on renal allograft function remain unknown.

Methods

2925 blood samples from 98 kidney transplant recipients obtained at eight consecutive visits during the first post transplant year were analyzed for CMV/BKV/TTV/EBV load by qPCR. Clinical characteristics, including graft function (eGFR), were collected in parallel.

Results

With 96.8 % and $1.46*10^6$ copies/mL, TTV had the highest prevalence and viral loads among other analyzed viruses, respectively. Of interest, we observed a significant increase in viral load and prevalence of TTV reactivation measured before and 3 months after transplantation, which was followed by a steadily TTV load decrease during the later post-transplant visits. We found 25.8 % of combined reactivation between TTV and BKV, 15.2 % between TTV and CMV and 7.6 % between TTV and EBV. Combined reactivation of TTV with CMV, BKV or EBV did not lead to a significant impairment of the renal function defined by eGFR at month 12.

Conclusion

TTV reactivation is increased after transplantation demonstrating the highest prevalence within the analyzed latent viruses. Combined reactivation of TTV with all three viruses was found but did not lead to significant renal graft impairment.

P06-16

Cognitive Profile Of Kidney Transplant Patients

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Introduction

Association of cognitive impairment with chronic kidney disease especially in Enstage-renal-Disease has been reported over the last decade [1,2]. Data about cognitive function in transplanted patients is rare [3]. Individuals after kidney transplantation are more likely to be affected by cognitive impairment than age-matched comparison groups. The goal of our study is to examine the extent of cognitive impairment after kidney transplantation and to derive a distinct profile of cognitive function using standard neurocognitive tests, as this is important for developing management strategies.

Methods

Participants completed standardized neurocognitive assessment and were then classified as having no, mild, moderate or severe cognitive impairment based on an established algorithm. For statistical analyses, we compared two groups (no vs. any impairment) using χ^2-tests for dichotomous variables, and unpaired (between groups) as well as paired (between domains) t-tests for continuous variables.

Results

59 patients (43 men, 16 women, mean age 55±13 yrs) took part in the study. 26 (44%) of the patients had no, 9 (15%) a mild, 15 (25%) a moderate and 9 (15%) a severe cognitive impairment. There was no difference between groups in duration on dialysis before transplantation ($t(57) = -0.82$, $p = .208$) or in time since transplantation ($t(57) = -1.04$, $p = .150$). The group with cognitive impairment performed significantly worse in the cognitive flexibility domain than in the other domains (comparison with verbal memory $t(32) = 2.93$, $p = .015$; with attention $t(32) = 3.69$, $p < .010$).

Conclusion

The prevalence of cognitive impairment is common in non-demented patients after kidney transplantation and appears to be intermediate between dialysis patients and the normal population. The duration of dialysis before transplantation has no influence on cognitive performance. Creating a neurocognitive profile is helpful and important, as the therapy for the treatment of cognitive impairment is based on the cause of the disease, based on the reduction of vascular risk factors (consistent antihypertensive therapy, optimal adjustment of any existing diabetes, etc.) and seems to be of crucial importance and priority

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P06-18

Donor Proteinuria And Allograft Function In Kidney Transplantation: Short- And Long-Term Results From A Retrospective Cohort Study

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Third And Forth Kidney (Re)Transplants: Increased Risks By Transplantation Into The Ipsilateral Iliac Fossa?

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Introduction
When planning retransplantation of the kidney it is generally preferred to select the un-operated, contralateral site for implantation. In case of a third or forth transplant the kidney will have to be transplanted into an illiac fossa which has previously been dissected, posing additional surgical challenges. The present study investigated whether re-transplantation into a previously operated iliac fossa poses increased risks.

Methods
This is a retrospective analysis of a prospectively maintained database. During a 20 year period (01.01.2001 - 01.01.2021) 108 retransplants have been performed. 82 cases with complete data were included. In 18 cases (study group - SG) that kidney-retransplant was performed in the ipsilateral iliac fossa, i.e. in a previously operated field, while in 64 cases (control group - CG) the kidney was transplanted into the contralateral iliac fossa, i.e. in a region that had not been dissected before.

Results
The SG had a higher proportion of male recipients compared to CG (61% vs. 28%). The proportion of live donor transplants was comparable (SG 22% vs. CG 17%). Duration of surgery was longer in SG (median 219 min)

Introduction
Donor proteinuria is a common but rarely evaluated characteristic in today's kidney transplant allocation process. While proteinuria after kidney transplantation is a risk factor for impaired graft function and survival, the long-term effects of donor proteinuria in kidney transplantation have not been evaluated yet. Aim of this study was to investigate the impact of donor proteinuria on long-term outcome after kidney transplantation.

Methods
This single centre study included all patients, who received a renal allograft between 2006 and 2016. Patients were stratified into two groups: (1) receiving a graft from a donor without proteinuria (DP-) and (2) receiving a graft from a donor with proteinuria (DP+), defined as any positive result on routine dipstick testing. Primary endpoint was a composite endpoint consisting of graft loss and patient survival. Secondary endpoints included graft function (eGFR), protein-excretion, delayed graft function, biopsy proven rejection and occurrence of cardiovascular events. Additionally, a subgroup analysis within the DP+ cohort was conducted to investigate the impact of DP severity.

Results
A total of 587 patients were found eligible, of whom 213 (36.3%) received a DP+ graft and 374 (63.7%) received a DP-organ. Donor characteristics were comparable with a similar kidney donor risk index. At 36 months, there was no difference in the primary composite endpoint (log rank test $p = 0.377$) or graft function and DP+ was not associated with graft loss (hazard ratio 0.87, 95% confidence interval 0.48 – 1.58) or patient survival (hazard ratio 1.57, 95% confidence interval 0.87 – 2.82). However, subgroup analysis showed a significant reduction in eGFR in the DP+ group between high and mild proteinuria ($p < 0.001$).

Conclusion
DP did not adversely affect patient or graft survival over a period of 36 months. Nevertheless, differences in the secondary endpoint analysis revealed a trend towards decreased eGFR values in DP+ patients, especially in subgroups with severe proteinuria. Therefore, the underlying results suggest caution in the allocation of kidneys from highly proteinuric donors.

compared to CG (median 165 min). Despite a lower hemoglobin concentration 24 hrs post op in SG, the need for RBC transfusion was comparable (SG 5,9% vs. CG 4,8%). DGF occurred more often in SG (47%) compared to CG (28%). Surgical complications were comparable in both groups with the exception of postoperative bleeding (SG 33%, CG 6%), One death occured in each group (SG: hemorrhagic shock 1.POD; CG - MOF 12.POD). Graft and patient survival were comparable between both groups (1-yr patient survival SG 89% vs CG 97%, 1 year graft survival SG 82% vs CG 89%).

Conclusion

While transplantatation into a previously operated recipient site may pose surgical challenges as reflected by a longer duration of surgery, the long-term results are comparable to those patients where, in case of a first retransplant, the naive, untouched contraleral illiac fossa may be used for implantation.

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P06-20

Detection Of Subclinically Active Antibody-Mediated Rejection Using dd-cfDNA Following An HLA-Incompatible Living Donor Kidney Transplantation

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Introduction

Given the existing organ shortage, HLA-incompatible living donor kidney donation is an important option for early kidney transplantation. To minimize the risk of antibody-mediated rejection, desensitization is required preoperatively. Donor-derived cell-free DNA (dd-cfDNA) is becoming increasingly important as a biomarker for the early detection of graft injury after renal transplantation, particularly in the context of antibody-mediated rejection.[1,2,3]

Methods

An account is given of a 52-year-old female patient affected by ADPKD who underwent a living kidney transplantation donated by her husband. Because of a preexisting DSA (DR 7), preoperative desensitization was performed using five plasma separations in combination with immunoglobulin administration. Induction therapy was performed with ATG. The patient received tacrolimus, MMF, and steroids as baseline immunosuppression.

Results

After desensitization, the pre-existing DSA could no longer be detected preoperatively and the transplantation could be performed successfully. Postoperatively, good graft function developed (creatinine 90-110 µmol/l). On postoperative days 15 and 27, preexisting DSA was again detectable, and a de novo DSA (DQ2) was detected once on postoperative day 15. With continued stable graft function (creatinine 80 µmol/l), a significant increase in dd-cfDNA of 2.61% was seen as an indication of severe graft damage.

In the immediately performed biopsy, acute T-cell mediated rejection Banff IIa was detected in addition to active antibody-mediated rejection. In addition to renewed plasma separations (5x), there were three more administrations of ATG and a steroid pulse. A control biopsy taken six weeks later showed significant regression of the rejection.

Conclusion

In the case described here, the detection of markedly elevated dd-cfDNA allowed early diagnosis and the successful treatment of a severe rejection following a living donor kidney transplantation.

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P06-22

Tumor Incidence And Immunosuppressive Therapy Following Kidney Transplantation - A Retrospective Monocentric Analysis

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Introduction

Tumor incidence after renal transplantation (NTX) is increased due to the immunosuppressive therapy. Therefore, risk-adapted long-term immunosuppression strategies seem a reasonable concept and should be investigated.

Methods

934 recipients of kidneys from deceased donors transplanted between 1999 and 2016 were retrospectively examined for the incidence of benign and malignant tumors. Due to a risk-based immunosuppressive approach in our center, three different immunosuppressive therapy regimens (IR) could be compared: High Risk (HR): HLA mismatch (HLA-B+-DR>2 or DR=2) or PRA>5% and retransplantations: ATG for induction, tacrolimus, MMF, and steroids (n=280; 30%, age 47.9±12.1, 38.0% female), low-risk (LR): ciclosporin, MMF, and steroids (n=395; 42.3%, age 48±12.5, 36.0% f.), and Eurotransplant Senior Program (SP): same as low-risk, plus basiliximab for induction (n=259; 27.7%, age 68.0±3.2, 28.6% f).

Results

In a median observation period of 10 (2-23) years, n=234 (25%) patients had 392 tumors after a median of 5 (2-21) years, of which n=275 (70.2%) were malignant and n=89 (22.7%) benign (of which 63 were tumors of the skin, 70.8%). N=28 (7.2%) were carcinomata in situ of the skin. Most malignant tumors were found in the SP group (n=110, 28.0%), followed by LR (n=98, 25.0%) and HR

(n=67, 17.1%). The rejection rates were 32.6% in SP, 50% in LR and 17.4% in HR. 19.7% (n=46) of the patients with tumors died (SP: n=15, 32.6%; LR: n=23, 50.0%; HR: n=8, 17.4%). In addition to skin tumors (n=169; 61.5%), renal cell carcinomas represented the most common entity of malignant tumors (n=21; 7.6%), followed by tumors of the gastrointestinal tract (n=20; 7.2%) and prostate carcinomas (n=19; 6.9%). This is followed by tumors of the respiratory tract (n=13; 4.7%), tumors of the female genitalia (n=10; 3.6%), post-transplant lymphomas (n=9; 3.3%), tumors of the urogenital tract (n=7; 2.5%), sarcomas (n=3; 1.1%), enoral tumors (n=2; 0.73%), and tumors of the central nervous system (n=2; 0.73%).

Conclusion

As little as 5 years after kidney transplantation, up to a quarter of patients are affected by tumors in particular of the skin. More potent immunosuppressive therapy did not appear to have a negative impact on tumor incidence, but higher rejection rates seem to be associated with increased tumor incidence, as does older age.

Poster Session 07: Structural, Process, Outcome Quality Of A Transplant Centre / Ethics / Psychosomatics

P07-01

Impact Of Structured Donor Identification And Multi-Professional Care On Organ Donor Management At Leipzig University Hospital's Transplant Coordinator Unit

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Introduction

In 2019, due to the amendment of the German Transplantation Act (TPG)[1], a medical-led Transplant Coordinator Unit was established at Leipzig University Hospital. This team, composed of nurses, physicians and psychologists, ensures a qualified care of (potential) donors and their relatives across all intensive care units of

the hospital. In 2021, the recognition and documentation of potential donors and care needs (TxB-Screen)[2] were implemented and subsequently supplemented with the standardisation of organ donor identification and management processes. Here, we investigate the effectiveness of these structural interventions on the number of managed organ donors and support of family members.

Methods

The 3-year periods 2016 to 2018 and 2020 to 2022 (before and after the amendment of the TPG) were compared regarding the number of the organ donations realised at Leipzig University Hospital. Additionally, an earlier annual period (first half of 2021) of the implementation of the structural measures was compared with a later period (latest six months, i.e. December 2022 to May 2023) regarding the number of potential donors identified and the number of family members cared for by the Transplant Coordinator Unit.

Results

In the period before the amendment of the TPG (2016 to 2018), 25 organ donations were realised, while in period thereafter (2020 to 2022) 38 were achieved (+52%). Following the commencement of implementing structural measures, in the first half of 2021, a total of 82 potential donors were identified in the TxB-Screen, 31 of whom were identified as requiring and being provided with multi-professional care. In comparison, during the latest available 6-month period (December 2022 to May 2023), the Transplant Coordinator Unit already identified 383 potential donors (+367%) and provided appropriate care in 87 cases (+181%).

Conclusion

The implementation of a dedicated Transplant Coordinator Unit with structured procedures for donor identification and subsequent multi-professional care seems to represent an appropriate intervention to ensure quality of care and reliable donor identification in accordance with the TPG.

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P07-04

Prevalence Of Obesity In Patients On The Waiting List For Kidney Transplantation

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Introduction

Obesity is one of the leading causes for the development of chronic kidney disease and is furthermore leading to a higher morbidity and mortality after kidney transplantation. To avoid pre- and postoperative morbidity on the waiting list, bariatric surgery could be an approach. The aim of this study was to calculate the prevalence of obesity in patients listed for a kidney transplantation, to analyze associations with age, gender and other comorbidities and to estimate the number of patients who would be eligible for bariatric surgery at our transplant center.

Methods

This retrospective study included 274 patients listed for a kidney transplant at a university transplant center between November 2018 and January 2020. A database was build comprising the transplantation status, comorbidities, BMI and other patient specific variables. Statistical analysis was performed testing for correlations between obesity and comorbidities.

Results

From the patients on the transplantation list 79,3% of the patients (n=215) had a BMI < 30 kg/m^2 and 20,7% (n=56) had an BMI ≥ 30 kg/m^2. The median BMI of transplantable (T) patients on the list was 25,8 kg/m^2. The incidence of obesity was 20,7 %. There was a significant correlation between the BMI and arterial hypertension (p=0,047), and diabetes mellitus (p<0,001). There was no correlation between the status of the patient on the transplant list (T= transplantable, NT= not transplantable). Ten patients (18%) were identified, who met the criteria for a bariatric surgery.

Conclusion

There was a significant correlation of hypertension and diabetes and the BMI of the patients listed for kidney transplantation. Bariatric surgery should be explored as a treatment option for patients on the transplant list, as it can decrease the BMI and therefore facilitating kidney transplantation and improving post-transplant outcome.

P07-05

Vigilance Data In Organ Donation And Solid Organ Transplantation In Germany: Donor-Derived Disease Transmission From 2016-2022

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Introduction

Diligent reporting and analysis of all serious adverse event (SAE) and serious adverse reaction (SAR) cases can help to identify risks of transmitting donor-derived disease to transplant recipients. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is the delegated body assigned by the German competent authority (Federal Ministry of Health) responsible for the management of the national SAE/SAR system.

Methods

A special team of qualified physicians of the DSO analyzed all SAE and SAR reported to the DSO from January 1st 2016 to December 31st 2022. In case of a possible transmission of a disease to one or more recipients, an assessment of imputability was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).

Results

Between 2016 and 2022, 21060 organs were transplanted from 8519 donors. In the same period, the DSO received 543 SAE/SAR reports. 53 of the 543 reports (9,8%) were proven or probable (P/P) transmissions of infectious diseases, malignancies or other diseases to 75 recipients. 17 of 75 (17/74; 23 %) recipients died due to the transmitted disease. Infections were the most frequently reported P/P disease transmission occurrences (30/53; 57%). In 12 cases bacteria were responsible, in 10 cases fungi, in 7 cases viruses and in one case a parasite with together 6 attributable deaths. 16 cases (16/53; 30%) were P/P transmissions of malignancies to 22 recipients resulting in 11 attributable deaths (11/22; 50 %).

Conclusion

Donor-Derived disease transmission is a rare event (53/8519; 0,6 %), but when it occurs can lead to significant morbidity and mortality, especially when malignant diseases are transmitted [1], [2]. Reporting of SAE and SAR can identify possible risks in organ donation and solid organ transplantation and helps to improve donor characterization and to increase awareness of transmission events.

The authors would like to thank the entire SAE / SAR team for their great support in the preparation, editing and evaluation of the SAE / SAR reports.

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P07-06

Donor-Transmitted Cancer In Organ Donation And Solid Organ Transplantation In Germany From 2016-2022

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Introduction

Analyzing reported serious adverse events (SAE) and serious adverse reactions (SAR) is an essential part of an effective vigilance and surveillance system in organ donation and transplantation. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is assigned by the German Federal Ministry of Health to manage and monitor SAE and SAR. Donor-transmitted cancer (DTC) can pose an additional risk to the recipients with significant morbidity and mortality.

Methods

All incoming SAE and SAR reported from January 1st 2016 to December 31st 2022 related to a potential malignant disease were analyzed. A DTC was defined as a malignancy already present within the organ at the time of transplantation. The assessment of imputability as proven or probable (P/P) transmission was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).

Results

145 reports were analyzed. In 104 reports the final histopathological analyses showed a malignant tumour (104/145; 72%). 16 reports were classified as P/P DTC from the donor to one or more recipients. These 16 cases involved 22 recipients resulting in 11 attributable deaths (11/22; 50 %). These cases included three adenocarcinomas, two lymphomas, two melanomas, two renal cell carcinomas, two urothelial carcinomas, two neuroendocrine lung cancer, one pleural mesothelioma, one squamous cell carcinoma and one angiosarcoma. 0,19 % of the 8519 donors (16/8519; 0,19 %) transmitted a P/P cancer to 0,11 % of all recipients (22/20315; 0,11 %).

Conclusion

With careful donor screening, transmission of a malignancy to a recipient is a rare event, but when it occurs, tumor transmission can lead to significant morbidity and mortality [1], [2]. Reporting of SAE and SAR can identify possible risks in organ donation and solid organ transplantation and helps to improve donor characterization and to increase awareness of transmission events.

The authors would like to thank the entire SAE / SAR team for their great support in the preparation, editing and evaluation of the SAE / SAR reports

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P07-07

Single Center Retrospective Analysis Of Risk Factors Associated With Aged Kidney Transplants

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Is Preferential Treatment On The Kidney Waiting List Unethical?

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Introduction

The lack of a sufficient supply of cadaveric organs for transplantation in most countries makes living donation an important possibility. However, a willing living organ donor is rarely a good enough match to his or her partner who has developed an organ (mainly kidney) disease. One way to overcome this problem is a transplantation procedure involving two or more couples (cross-over-transplantation, serial transplantation). However, so far this possibility is quite underdeveloped in most countries, due to organizational and informational problems and legal restrictions. Mitigating the shortage may be achieved through living donation to the waiting list, which, though, will usually not happen, except the intended recipient gets a preferential treatment, i.e.: improving his/her position on the waiting list for cadaveric organs [1], [2], [3].

Methods

The effect of preferential treatment on the waiting times of all patients is derived by a mathematical model with realistic assumptions.

Results

This contribution shows that such a preferential treatment will definitively reduce the shortage. Whether it will be regarded as ethically tolerable depends on the relation between the degree of promotion and the effects on the waiting time of patients without a willing donor.

Conclusion

A scientifically supervised trial in cooperation with at least one willing transplant clinic is necessary to finally and empirically prove the theoretical conclusions of the

Introduction

The continued shortage of donated kidneys and an ever aging society have led to the consideration of older organs for transplantation. The use of older organs has helped in curtailing the organ shortage, but is associated with higher risk of delayed graft function (DGF), primary non function and acute rejection. Since the introduction of expanded criteria donor (ECD) guidelines in 2002, older organs (50-60) have been screened based on defined risk factors. We aimed at indetfying additional risk factors, which are associated with negative post-transplant outcome of the aged donor orgas. The insights gained should help physicians develop strategies for acceptance of aged donor organs, beyond ECD guidelines. Furthermore, novel strategies could be devised for pre-implant reconditioning of the aged organs for targeting risk factor associated deficits.

Methods

Our retrospective study includes donor and recipient data from 1251 transplantations, performed at Charitè Medical University, Berlin between 2015 and 2022. The donors were divided into three groups: young donors (YD) (<50years); middle-aged donors (MD) (50-60 years); old donors (OD) (>60 years). The donors were further subgrouped into standard sriteria donor (SCD), ECD and very old donors (VOD) (<70years) groups. Donor risk factors include cerebrovascular cause of death, creatinine levels ≥ 1.5mg/dl, hypertension, diabetes, cardiovascular diseases and ischemia time. Outcome data pertaining to acute graft rejection, DGF and graft survival were collected.

Results

We observed an increasing median age of donors in the past years. OD showed higher rates of DGF (34,1%), compared to YD (18,8%) and MD (19,2%). Incidence of DGF was indifferent between the OD and VOD groups. Likewise, OD and ECD transplants demonstrated similar outcomes in recipients above 60 years. Compared to the other donor groups, older donors with diabetes and hypertension showed worse graft outcome.

Conclusion

Transplantation of older organs show fewer shortcomings compared to younger organs in older recipients. Further, organs from older donor with diabetes and hypertension are potentially worthy targets for preimplant reconditioning.

paper. An important pillar for the ethical acceptance -- or not -- of preferential treatment is the opinion of patients on the waiting list.

This contribution does not stand in any connection to any company or product.

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P07-12

Long-Term Adaptation Requirements After Liver Transplantation: Changed Coping Tasks After The 1St Year After LTX

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Introduction

The study investigates the health-related quality of life and satisfaction with the care of patients after LTX.

Methods

With the approval of the Ethics Committee, all patients who underwent liver transplantation at the Transplant Centre of the University Medical Center Rostock from 08/2019 to 05/2022 were included in the study (LTX > 6 months). The questionnaire package consisted of: SCL-90 on subjective impairment due to physical and psychological symptoms, EQ-5D-5L on health status, SF12 on health-related quality of life. In addition, a clinical interview was conducted by telephone.

Results

37 patients were included, 32.4% female, mean age 57.9 years (SD 7.9), 6 (16.2%) died after LTX. Leading underlying disease: 43.2% HCC, 35.1% liver cirrhosis of ethyltoxic origin. 14 (45.2%) of the surviving patients returned the questionnaires. Massive reduction in health-related quality of life due to physical (SF12, M: -0.9185; SD: 0.88338) and psychological complaints (M: -0.6046; SD: 1.49811). 86.7% with significant pain, 25% of which was severe, and major limitations in coping with daily life. Although the impairments remained the same or decreased in the second year after LTX (N=14), the stress experience increased in all respondents due to the persistent or new deficits, especially mobility, pain, fatigue, lack of strength, cognitive deficits (EQ-5D-5L). 57.1% of the patients described reduced hope, decreasing confidence in improvement after the first year, 42.9% disappointed expectations after repeated everyday trials and experiences of failure. Despite primarily very high satisfaction with the treatment and the information provided during the listing and perioperatively, 35.7% expressed insufficient information on lifestyle (sports, travel, sexuality) and uncertainty regarding necessary hygiene measures (nutrition, contact behaviour) after the first year after LTX.

Conclusion

The small sample size limits the significance considerably. However, the results point to the need for long-term support, oriented towards psychoeducational, multimodal approaches to chronic pain therapy, which promotes coping and reorientation of transplanted patients, especially in terms of realistic goals.

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