7th - 9th November 2024

Transplant International

Abstracts of the 33rd Annual Meeting of the German Transplantation Society, Freiburg im Breisgau, Germany

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Introduction

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Die 33. Jahrestagung der Deutschen Transplantationsgesellschaft findet in diesem Jahr vom 07.-09. November in Freiburg im Breisgau statt. Wir heißen alle TeilnehmerInnen herzlich Willkommen und freuen uns auf einen regen fachlichen Austausch und spannende Diskussionen rund um das Thema Transplantationsmedizin.

Neben den Plenarsitzungen zu den Themen DCD, Organrecruitement und Xenotransplantation findet eine Vielzahl an wissenschaftlichen und Postersitzungen statt. Neben den klassischen wissenschaftlichen Sitzungen bietet die Jahrestagung mit dem großen Angebot von mehreren Masterclass-Kursen, einem Curriculum Organentnahme bis hin zum OP-Trainingskurs Organentnahme und den Hands-On Kursen u.a. zur ex-vivo Perfusion ausgezeichnete Möglichkeiten zu Aus- und Weiterbildung im Feld der Transplantationsmedizin. Mit Programmpunkten zu "Women in Transplantation" wird den besonderen Herausforderungen durch Gender-Aspekte und der Vereinbarkeit von Familie und Beruf in der Transplantationsmedizin Rechnung getragen.

Wir freuen uns Sie in Freiburg begrüßen zu dürfen!

The 33rd Annual Meeting of the German Transplantation Society takes place this year from November 7 to 9 in Freiburg/Breisgau. We warmly welcome all participants and look forward to a lively professional exchange and exciting discussions in the field of transplantation.

In addition to the plenary sessions on DCD, organ recruitment and xenotransplantation, there will be a large number of scientific and poster sessions. In addition to the scientific sessions, the annual meeting offers excellent opportunities for education and training in the field of transplantation medicine with a wide range of masterclass courses, a curriculum on organ harvesting, a surgical training course on organ harvesting and hands-on courses, including ex-vivo perfusion. With program items on "Women in Transplantation", the special challenges posed by gender aspects and the compatibility of family and career in transplantation medicine will be taken into account.

We look forward to welcoming you in Freiburg!

Table of contents

Programme

Thursday, 07 November 2024

08:00-09:30	Poster Session 01: Liver	Commission Session: Heart/lung	Commission Session: Kidney	Organ Donation	Commission Session: Ethics
09:30-10:00	Break				
10:00-11:05	Opening Ceremony				
11:15-12:30	Plenary Session I: Organ Donation-DCD				
12:30-12:45	Break				
12:45-13:45		Lunch Symposium	Lunch Symposium	Lunch Symposium	
13:45-14:00	Break				
14:00-15:30	ABOi - Cross-Over/ Kidney Exchange Program	Heart transplantation in general	Meeting of the Young Transplantation Medicine Working Group 01	Poster Session 02: Immunology	
15:30-16:00	Break				
16:00-17:30	Basic Science	Master Class I: Best medical treatment	Register session SOLKID-GNR	Liver allocation	Commission Session: Psychology/ psychosomatics
17:30-18:00	Get Together in the exhibition area				
18:00-20:00	DTG General Meeting				

Friday, 08 November 2024

08:00-09:30	Mentoring Breakfast	Lungs in general	Commission Session: Organ removal	Poster Session 03: Kidney rejection Immunosup-pression	Commission Session: Liver/ intestine
09:30-09:45	Break				
09:45-10:30		Breakfast Symposium	Breakfast Symposium	Breakfast Symposium	
10:30-11:45	Plenary Session II: Organ suitability/organ recruitment				
11:45-12:00	Break				
12:00-13:00		Lunch Symposium	Lunch Symposium	Lunch Symposium	Working Group Pediatrics
13:00-13:15	Break				
13:15-14:45	Immunology	Ethics	Master Class II: Allocation	Poster Session 04: Kidney in general / Pancreas	News from the work on guidelines 01
14:45-15:15	Break				
15:15-16:30	Social law issues after transplantation	Transplant registry	Kidney trans-plantation for underlying ge-netic disease	HTX congenital vitia	Organ donation initiative
16:30-16:45	Break				
16:45-18:00	Preconditioning	Commission Session: Immunology	Women in Transplantation	Complication management after liver transplantation	Commission Session: Pancreas

Saturday, 09 November 2024

08:30-09:45	Plenary Session III: Xenotrans-plantation				
09:45-10:30	Award presentations				
10:30-10:45	Break				
10:45-11:30		Brunch Symposium	Brunch Symposium	Brunch Symposium	German Transplant Study Group
11:30-11:45	Break				
11:45-12:45	Infectology	Pancreas transplantation: state-of-the-art or obsolete model	Master Class III: Living donation	Poster Session 05: Basic Science	News from the work on guidelines 02
12:45-13:00	Break				
13:00-14:00	(Kidney) transplantation of highly immunized patients	Surgical challenges in transplant surgery	Meeting of the Young Transplantation Medicine Working Group 02	Poster Session 06: Lung	Psychology/ Psychosomatics
14:00-14:30	Closing and invitation DTG 2025				

Oral Presentations

Organ Donation

WS01-03

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Initial Experience Of Virtual Crossmatch Implementation In Germany

Introduction
Virtual crossmatch (vXM) started in all Eurotransplant (ET) member states on 2023-01-23. This required organisational and technical changes: Due to ambiguity resulting from current technical constrains in fast HLA typing, the HLA-laboratories report all possible HLA-alleles identified in a donor (A, B, C, DRB1, DRB3, DRB4, DRB5, DQB1, DQA1, DPB1, DPA1) as an HML file to ET. ET converts this into 2-field-typing respecting CIWD 3.0 catalogue and 18th HLA nomenclature workshop definitions. Laboratories check the correctness of this automatic conversion by ET and adjust in case of unexpected deviations in phenotypes. Hereafter all kidney, pancreas and intestine waiting list candidates with unacceptable antigens or alleles against the donor are deselected from the allocation process for this donor. The vXM is complemented by a physical crossmatch (LCT) prospectively performed for immunized recipients and retrospectively for all others.

Methods
For all German organ donors from 2023-4-24 to 2024-06-03 (1) HLA-HML-file uploads were analyzed to identify any technical limitations and (2) results of vXM and LCT were compared to identify any inconsistencies.

Results
(1) For 1124 donors 1152 HML-files were uploaded. 1060 files (92%) required no major manual correction, 82 files (8%) needed manual adjustment due to complex HLA-issues. Switch to manual backup occurred in 10 cases (1%). Mean duration for completing vXM was 6 min. (including all manual work). (2) 1808 LCT-tests were performed for allocated recipients with negative vXM. In 22 cases (1.2%) a positive result had impact on allocation (8 autoimmune issues, 5 Antibody data not entered well, 1 viral infect, 1 non-HLA-Antibodies, 4 unexplainable but not HLA, 1 possible overlap of HLA-epitopes – B-cell test failed: interpretation impossible, 2 pending investigation).

Conclusion

Since implementation of vXM quality of donor HLA-typing improved and is standardized. For LCT an excellent prediction of results exists by vXM. Further quality control is necessary for discussion about future LCT indication.

WS01-04

Effect Of Donor Resuscitation On Early Liver Graft Survival In Donation After Brain Death

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Introduction
The effect of cardiac arrest and resuscitation on graft survival after Donation after Brain Death (DBD) has not been extensively researched. The impact of donor cardiac arrest on graft survival post-Donation after Brain Death (DBD) is influenced by several critical factors. Cardiac arrest introduces risks to graft viability due to ischemia, which can cause significant tissue damage.

Methods
We present preliminary data from 1563 consecutive liver transplants from a single center from December 1998 to December 2020. We conducted both univariable and multivariable analyses to identify predictive factors for graft survival in organs from donors who underwent resuscitation compared to those who did not.

Results
The median age of donors at the time of organ donation was 54 years, with an interquartile range (IQR) of 50-58 years. Donors who underwent reanimation exhibited a median duration of cardiac arrest of 152 minutes (IQR 120-184 minutes) compared to virtually none in those not reanimated.

We identified 93 (6%) DBD after resuscitation. Median resuscitation time was 10 (1-90) minutes. 3-month and 1-year graft survival for recipients of post- resuscitation grafts was 90% ,83% and 85%, 73.5% for no post-resuscitation donor grafts. (log rank p = 0.18). In the multivariable analysis donor age was identified as a risk factor for graft survival (HR=1.014; 95% CI: 1.009-1.019). Notably, extended left liver splits were exclusively performed in non-reanimated donors (3.3%).

During a median follow-up period of 3.5 years (IQR 2.0-5.0 years), similar re-transplantation rates were observed between reanimated and non-reanimated groups, 18.1% and 18.0% respectively, suggesting comparable long-term graft viability.

Conclusion
The use of post-resuscitation grafts is feasible. Thoughtful selection of these donors represents a prudent strategy for broadening the donor pool.

WS01-05

Vigilance Data In Organ Donation And Solid Organ Transplantation In Germany: Donor-Derived Disease Transmission From 2016-2023

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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 2023. 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 2023 9771 donors in Germany donated postmortem organs to 27919 recipients. In the same period, the DSO received 612 SAE/SAR reports. 68 of the 612 reports (11 %) were proven or probable (P/P) transmissions of infectious diseases, malignancies or other diseases to 95 recipients. 20 of 95 (20/95; 21 %) recipients died due to the transmitted disease. Infections were the most frequently reported P/P disease transmission occurrences (41/68; 60%). In 18 cases bacteria were responsible, in 14 cases fungi, in 8 cases viruses and in one case a parasite with together 7 attributable deaths. 19 cases (19/68; 28%) were P/P transmissions of malignancies to 27 recipients resulting in 13 attributable deaths (13/27; 48 %). Furthermore 8 P/P transmission of others diseases to 10 recipients occurred, none of them died.

Conclusion

Donor-Derived disease transmission is a rare event (68/9771; 0,7 %), 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.

Acknowledgment

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

References

[1] Kaul DR, Vece G, Blumberg E, et al. Ten years of donor-derived disease: A report of the disease transmission advisory committee. *Am J Transplant*. 2021;21(2):689-702. doi:10.1111/ajt.161711.

[2] Böhler K, Rahmel A, Barreiros AP. Vigilance Data in Organ Donation and Solid Organ Transplantation in Germany: Six Years of Experience 2016-2022. *Transpl Int*. 2023;36:11610. Published 2023 Sep 4. doi:10.3389/ti.2023.11610

WS01-07

En-bloc Nephrectomy During Organ Procurement Leads To A Significant Reduction In Organ Extraction Time

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Introduction

In organ procurement, during the time interval between the start of the cold perfusion and the extraction of the organs from the body (extraction time), the temperature of the organs remains suboptimal leading to further ischemic damage. Studies from the USA and Netherlands, focusing on donation after cardiac death, have shown a large variation of the extraction time during procurement and that a prolongation leads to a higher rate of delayed graft function. We therefore propose that the en-bloc nephrectomy during organ procurement can shorten the extraction time and could improve the transplantation outcome.

Methods

The extraction time of 242 procurements between January 2017 and December 2023 were analyzed. The time difference between the first extracted kidney of either en-bloc or separately extracted kidneys was compared. In addition, a multivariate, linear regression model was used to identify further variables influencing the extraction time.

Results

Of the 242 procurements, 157 kidneys were extracted en-bloc (64.9%) and 85 kidneys separately (35.1%). The extraction time of en-bloc procured kidneys was significantly shorter than those of separately procured kidneys (median: 44 vs. 60 minutes; p <0.001). The regression

model showed a prolongation of the kidney extraction time (set as constant of 44 minutes) when thoracic organs (+7 minutes), the liver (+11 minutes), and/or the pancreas (+12 minutes) were procured and the en-bloc nephrectomy was able to significantly reduce the extraction time by 14 minutes.

Conclusion

The en-bloc nephrectomy significantly reduces the extraction time during organ procurement, thus, reducing the time of suboptimal cooling of the organs. Further evaluation will show whether this can positively influence graft survival.

ABOi - Cross-Over/ Kidney Exchange Program

WS02-02

Increased Risk Of Acute Antibody-Mediated Rejection Despite Long-Term Compromised B Cell Repopulation After Rituximab Induction In Blood Group Incompatible (ABOi) Living-Donor Renal Transplantation

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Introduction

An increased risk of acute antibody-mediated rejection (ABMR) has been described after ABOi renal transplantation [1,2]. To detect long-term effects of rituximab induction on graft outcome in ABOi renal transplantation, we analyzed HLA antibody formation, clinically relevant immune parameters and protocol biopsies in a prospective renal transplant study up to 5 years posttransplant.

Methods

Mononuclear cell subsets (peripheral blood; protocol biopsies) and in-vitro T and B cell responses were assessed in 85 renal transplant recipients (living donation: n=25 ABOi (with rituximab induction) and n=30 ABO compatible (ABOc); deceased donation (DD): n=30, ABO compatible). IgG anti-HLA antibodies were assessed by single antigen assay in ABOc and ABOi recipients.

Results

In ABOi patients, an increased frequency of biopsy-proven acute rejection was found only in the 3-12 month posttransplant period (P=0.003 vs. ABOc and DD). A significantly increased frequency of ABMR was detected at 5 years (P=0.008 vs. ABOc and DD). After rituximab induction in ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years together with impaired in-vitro B cell responses (P=0.010, T-dependent; P=0.053, T-independent) at 2 years (P=0.019 vs. ABOc). Cell subset analysis in protocol biopsies showed 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. IgG anti-HLA antibody formation was not significantly different between ABOi and ABOc patients up to 5 years posttransplant.

Conclusion

Rituximab induction in ABOi patients induced a long-term profoundly delayed B cell repopulation together with compromised B cell responses. This resulted in complete B cell depletion in protocol graft biopsies at 3 months only but even upregulated T cell, macrophage

und plasma cell counts at 1 year coinciding with an increased acute rejection frequency between 3 and 12 months posttransplant. Rituximab induction in ABOi patients did not affect IgG anti-HLA antibody formation.

This study was supported by Astellas and Novartis. **ClinTrials.gov** NCT01136395; **EudraCT No.:** 2009-012198-36.

References

[1] de Weerd AE and Betjes MGH: ABO-incompatible kidney transplant outcomes. A meta-analysis. Clin J Am Soc Nephrol 13: 1234-1243, 2018

[2] Scurt FG, Ewert L, Mertens PR, Haller H, Schmidt BMW and Chatzikyrkou C: Clinical outcomes after ABO-incompatible renal transplantation: a systematic review and meta-analysis. Lancet 393: 2059-72, 2019

Heart Transplant In General

WS03-04

Assessment Of Intra-Patient Variability Of Tacrolimus On Fibrotic Plaques In Cardiac Allograft Vasculopathy After Heart Transplantation

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Introduction

Intra-patient variability (IPV) of tacrolimus (TAC) after solid organ transplantation is common and associates with poorer outcome after liver and renal transplantation [1]. In heart transplanted (HTx) patients, the relevance regarding prognosis and angiographic cardiac allograft vasculopathy (CAV_{angio}), a major cause for mortality and morbidity following HTx, remains unclear. Intracoronary imaging has shown that, beyond intimal hyperplasia, the prevalence of fibrotic plaques is common after HTx and associated with prognostically relevant stenosis and CAV progress [2]. With this study we aimed to evaluate the association of TAC-IPV with the prevalence of fibrotic plaques in routinely performed optical coherence tomography (OCT) during angiographic follow-up.

Methods

In a cohort of 54 consecutive HTx patients (87% male, post-transplant interval 8.2 $\pm$5.8 years), we assessed the entire TAC level data up to 2 years prior to OCT and excluded the first 6 months post-HTx. TAC-IPV was defined using: (1) percentage of measured TAC values within/above/below the recommended target range according to guidelines, (2) time in therapeutic range (TTR), (3) standard deviation (SD) of mean TAC, and (4) the co-efficient of variation. We quantified mean fibrotic arc, relative plaque length (RPL, % of analyzed vessel) and fibrotic plaque load (FPL, mean arc*RPL) by OCT.

Results

TAC measurements 20.6$\pm$6.4 months prior to OCT/angiography, with an average of 27 measurements/patients were included. Fibrotic plaques were present in 64.8% of patients. Patients with CAV_{angio} had a higher prevalence of fibrotic plaques (81.5% vs. 48.2%, p=0.01). Patients with <80% of measurements within range and TTR <65% had higher FPL (p=0.003 and p=0.03, respectively). Linear regression analysis showed a correlation between the percentage above the targeted range and mean fibrotic arc (beta 0.40 [0.06-0.95], p=0.03 and 0.37 [0.01-0.91], p=0.046, respectively). Logistic regression showed a predictive value of SD>median regarding high FPL (OR 5.50 [1.15; 26.41], p=0.03).

Conclusion

TAC-IPV was associated with fibrotic plaque parameters in OCT. TAC-IPV might detect HTx patients at higher risk for CAV.

References

[1] Coste, G, Lemaitre, F, 2022, 'The Role of Intra-Patient Variability of Tacrolimus Drug Concentrations in Solid Organ Transplantation: A Focus on Liver, Heart, Lung and Pancreasl', Pharmaceutics, 2022;14(2):379, doi:10.3390/pharmaceutics14020379

[2] Orban M, Dischl D, Müller C, et al. 2021, 'Analysis of Fibrotic Plaques in Angiographic Manifest Cardiac Allograft Vasculopathy in Long-term Heart Transplanted Patients Using Optical Coherence Tomography.', *Transplant Direct*. 2021;8(1):e1266, doi:10.1097/TXD.0000000000001266

WS03-05

The Effect Of Transplant Center Volume On Outcome After Heart Transplantation – A Retrospective Study Of The German Transplant Registry

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Introduction

The aim of this study was to assess the association between volume of annual heart transplantations performed in German transplant centers and the short-term outcome of our recipients.

Methods

Utilizing the German transplant registry, we conducted a retrospective analysis of 3,854 patients who underwent heart transplantation (HT) from 2006 to 2016 applying the newly introduced minimum volume standards of The Federal Joint Committee (*Gemeinsamer Bundesausschuss GBA*). Centers who never performed less than mean 10 HT annually considering 3-year intervals were considered high-volume centers; centers that at least once performed less than mean 10 HT annually within 3 year intervals were considered medium-volume centers and centers that constantly performed less than mean 10 HT annually within 3 year intervals were considered low-volume centers.

Results

The mean age was 52 years (39.4 – 59.0 years). 76.0% of recipients were male; 54.1% of donors were male, mean donor age was 40.6 $\pm$ 15.2 years. 2,823 (73%) patients were transplanted at high-volume centers (n=9); 696 (18%) patients were transplanted at medium-volume centers (n=7); 335 (9%) at low-volume centers (n=12). Compared to low-volume centers, patients transplanted at high-volume centers were younger (51.5 vs. 53.9 years, p=0.004), experienced longer ischemic times (204 vs. 199 min, p=0.003), had lower recipient BMI (24.3 vs 25.1 kg/m^2, p=0.011), and were more likely to be listed in a high urgency status (84.4% vs. 66.0, p<0.001). The 1-year survival was significantly better in high-volume centers when compared to low-volume centers (76.8%, CI 297-306 days vs. 64.5%, CI 247-279 days, *p*<0.001).

Conclusion

The outcome after heart transplantation depends on the center volume.

Basic Science

WS04-03

Proof Of Concept: Endothelial Cell Based Ex Situ Therapy Treating End-Stage Lung Diseases

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Introduction
Increasing incidence of end-stage lung disease requiring lung transplantation is accompanied by growing discrepancy between organ donors to recipients. Ex situ lung perfusion (ESLP) was developed to expand the donor pool, now also used for regenerative approaches. As endothelium (EC) plays an important pathogenetic role in these lung diseases, we developed a rat ESLP system to establish endothelial cell-based ex situ therapy to supplement or replace diseased EC with functional EC.

Methods
ESLP was established in transplantation-relevant rat strains with appropriate perfusion solutions (PL), analyzing perfusion parameters, thermal imaging, blood gas analysis, colloid oncotic pressure, lung weight gain, histological examinations and cytokines. In vitro, general effects of different PL on EC disintegration, subsequent integration of labelled EC and their regenerative potential in combination with ß-estradiol (ES) were analyzed. Subsequently, optimal protocol was applied in ex situ perfused rat lungs. After disintegration, labelled ECs were added to PL, and at the end of the experiment unlabeled, non-integrated ECs in PL were quantified by FACS, integrated ECs were detected by light sheet microscopy.

Results
ESLP showed significant differences in PL, but not between rat strains. Homogeneous lung perfusion with temperature- and perfusion-related metabolic activity was observed. Histologically, lung architecture was intact, without infarcts or hemorrhages. In regenerative ESLP, all PL led to EC disintegration, which was enhanced by the concentration-dependent ES addition. Microscopy confirmed vital integrated labelled EC into the native EC, whose confluence and barrier function were best regenerated in Steen solution. FACS analyses showed that only <1% of the labelled cells were washed out; labelled EC were detected throughout the whole rat lung.

Conclusion
General feasibility of this regenerative ESLP approach was proven and will be established for specific applications, e.g. using NO-overexpressing EC in pulmonary arterial hypertension. Successful implementation could enable both, donor pool expansion and autologous ex situ therapy, making transplantation unnecessary.

WS04-04

Free Heme And Hemopexin In Acute Kidney Injury In Patients After Cardiopulmonary Bypass And In Experimental Transient Renal Ischemia

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Introduction
Free heme is released from hemoproteins during hemolysis and ischemia and can be pro-inflammatory. Most studies on nephrotoxicity of hemolysis-derived proteins focus on free hemoglobin (fHb) which carries heme as a prosthetic group. Measurement of heme in its free non-protein bound form is challenging and not commonly used in clinical routine. In contrast to fHb, the role of free heme in acute kidney injury (AKI) after cardiopulmonary bypass surgery (CPB) is unknown.

Methods
Free heme in the circulation was determined at different time points during CPB using an apoperoxidase (apoHRP)-based assay in patients undergoing cardiac valve replacement (n=37). The concentration of plasma hemopexin (Hx) – a specific heme scavenger protein – was measured by ELISA. In C57BL/6 mice, the impact of

high circulating free heme levels on the development of AKI following transient renal ischemia and the therapeutic potential of Hx were investigated. C57BL/6 mice were subjected to bilateral renal ischemia/reperfusion injury (IRI) for 15 min and given free heme with or without subsequent scavenger therapy with Hx. Renal perfusion was measured using functional magnet resonance imaging (MRI) and renal tissue was analyzed by immunohistochemistry and qPCR.

Results

In patients, circulatory free heme during CPB predicted postoperative AKI. The increase in plasma free heme was paralleled by severe depletion of plasma Hx. In mice, renal IRI for 15min *per se* did not cause renal function impairment. However, additional administration of free heme in this model promoted overt AKI with reduced renal function, increased renal inflammation and reduced renal perfusion on functional MRI. Scavenger therapy with Hx attenuated AKI following mild renal IRI and free heme administration. In sham operated control mice without renal IRI, free heme did not cause AKI.

Conclusion

In conclusion, free heme is a predictor of AKI in CPB-patients and promotes AKI in transient renal ischemia. Depletion of Hx in CPB-patients and attenuation of AKI by Hx in the *in vivo* model encourage further research on Hx therapy in patients with high free heme levels during CPB.

WS04-05

Impact Of End-Stage Lung Diseases On The Immune Cell Composition In Lung Parenchyma

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Introduction

Lung transplantation (LTx) is the ultimate option for patients suffering from end stage lung diseases (ELD). Little is known about the immune cell composition in these diseased lungs that may be shaped by the underlying disease. Hence, we investigated the immune cell distribution of lung parenchyma obtained from different diseased lungs after explantation in the course of LTx and its potential influence on immunological tolerance.

Methods

Explanted lung parenchyma (n=57) was enzymatically digested; immune cell distribution was determined by flow cytometry. Lung tissue derived from patients with chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF) and PAH was compared to immune cell composition of healthy control parenchyma derived from non-tumor lung tissue. Meta data such as age, sex, PGD, immunosuppression were collected.

Results

Leukocyte proportions were generally enriched in diseased lungs (with >50% in COPD compared to non-tumor parenchyma. Lymphocytes represented the major leukocyte subsets in healthy and COPD lungs, while granulocytes were the majority in IPF and PAH lungs. In all diseases, CD4 and CD8 T cells, primarily tissue-resident memory (TRM), constituted the major lymphocyte population with particularly elevated levels in COPD and lowest levels in PAH and IPF tissue. COPD lungs showed highest proportions of $CD4^+$ T cells translating into highest $CD4^+/CD8^+$ ratio. Regulatory T cells were enriched in IPF lungs compared to other diseases and lowest in COPD lungs. Of note, while none of the patients with emphysema did develop PGD following LTx, few patients diagnosed with fibrosis or PAH developed PGD. We are currently correlating immune cell frequencies to PGD grades and other clinical parameters.

Conclusion

Our data conclusively prove that ELD imprint the immune repertoire, which is populating the lung parenchyma, indicating that each lung disease may be characterized by a unique immune cell compartment. A better understanding of the immune mechanisms involved in ELD will be essential for an adequate management of these diseases in the future.

WS04-06

A Step Toward Advancing Lung Xenotransplantation: Ex Vivo Lung Perfusion Of Genetically Modified Pig Lungs

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Introduction

Lung transplantation is the gold standard and the only curative treatment for chronic and acute lung failure. Although conservative therapy provides only symptomatic relief and slows disease progression, and ECMO therapy is restricted to weeks of use, the absence of viable alternatives is leading to patients dying on the waiting list or becoming too sick for life-saving transplantation. Therefore, novel therapeutic strategies are urgently needed, such as the use of pig lungs for xenogenic transplantation. The aim of this study was to establish a protocol with clinically approved ex vivo lung perfusion (EVLP) to lay the ground for future experiments aiming to improve xenotransplantation outcome by applying EVLP.

Methods

Lungs were retrieved from four GGTA1-KO pigs following euthanasia (DCD). After establishing perfusion of the pig with ice-cold Perfadex Plus solution trough the abdominal aorta and vena cava, the thoracic cavity was opened and the lung was flushed with ice-cold Perfadex Plus solution according to standard procedure via the pulmonary artery. After 2 hours of cold storage, the lungs were mounted on a clinically approved EVLP system primed with Steen solution. During the first hour of EVLP initiation, perfusion was gradually increased, and the organs were warmed to normothermia, and ventilation was started. Afterwards, lung recruitment according to the clinically approved procedure was performed. Organ performance was continuously monitored during the EVLP run.

Results

Lung retrieval without anticoagulation treatment of the donor was found to be feasible, and all four GGTA1-KO pig lungs could be perfused for 2 hours with Steen solution, exhibiting constantly low PVR. Lung recruitment using 100% O_2 resulted in significantly increased levels of dissolved oxygen up-to 600 mmHg, indicating perfectly functional lungs.

Conclusion

This study demonstrates the feasibility of using DCD GGTA1-KO pig lungs in an EVLP system primed with Steen solution as model to further study and advance xenogeneic lung transplantation.

WS04-07

Preliminary Results Of Normothermic Perfusion Of Alpha-Gal Knockout Porcine Livers With Human Blood In A Xenogeneic Model

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Introduction
The critical shortage of donor organs is a significant barrier in transplantation surgery. Porcine organs could be a viable solution, but Galactose-α(1,3)-galactose (αGal) on porcine cells triggers antibody-mediated hyperacute rejection in humans. Normothermic machine perfusion (NMP) using the Liver Assist™ (XVIVO) system provides a controlled setting for evaluating porcine organs. This study presents initial findings on NMP evaluation of livers from genetically modified pigs lacking αGal expression.

Methods
Three pigs were genetically modified using CRISPR/Cas9 to knockout the αGal gene (αGal-KO). Livers were procured following donation after circulatory death and perfused using the Liver Assist™ system with human blood (0 Rh^+) for 6 hours. Perfusion parameters and hyperspectral imaging (HSI) monitored liver perfusion. Flow cytometry analyzed donor blood and perfusate to confirm the absence of αGal epitopes and assess the release of porcine immune cells during NMP.

Results
NMP was conducted under physiological conditions, with average portal venous and hepatic artery flows of 523 ± 62 ml/min and 224 ± 74 ml/min, respectively. HSI showed homogeneous and stable graft perfusion over the entire 6-hour period, indicating effective blood distribution across the liver tissue. Flow cytometry identified a significant release of porcine immune cells into the perfusate, including NK cells (CD56), monocytes (CD14), T cells (CD4/CD8), and B cells (CD21). These cells remained in the perfusate until the end of NMP, indicating active immune cell shedding from the liver graft during perfusion. Flow cytometry of peripheral blood mononuclear cells (PBMCs) from αGal-KO pigs confirmed the absence of αGal epitopes.

Conclusion
Preliminary data indicate that liver perfusion using αGal-KO organs and a certified NMP system with human blood is feasible. The physiological perfusion parameters and HSI confirmed consistent and regular graft perfusion over the 6-hour period. Further research is necessary to explore the clinical significance of immune cell release and evaluate the potential of this approach as a bridging therapy.

Liver Allocation

WS05-05

MELD-Based Organ Allocation For Liver Transplantation Is Associated With Reduced Survival In Low Donation Countries – A Comparative Analysis Between Germany And The US

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Introduction
The allocation of donor livers based on the Model for End-Stage Liver Disease (MELD) score is the predominant practice in most countries worldwide. However, the impact of this policy in countries with low organ donation rates, such as Germany, remains uncertain.

Methods
Waiting list survival and survival after liver transplantation in Germany (2003-2016, MELD implementation 12/2006) and the US (1999-2016, MELD implementation 02/2002) were analyzed using data from the Germany Transplant registry and UNOS registry. A comprehensive cohort of 196,039 waiting list registrations and 108,199

liver transplantations was used for this retrospective analysis.

Results

Waiting list mortality did not improve after the introduction of MELD-based allocation in Germany (OR 0.97, 95% CI: 0.91 - 1.03). Moreover, survival after transplantation deteriorated in Germany (three-year patient survival preMELD 69.3% vs. MELD 65.3%, p < 0.001). Contrarily to this, an improvement in both waiting list mortality (OR: 0.73, 95% CI: 0.71-0.75) and survival after transplantation (preMELD 75.3% vs. MELD 80.5%, p < 0.001) was found after the implementation of MELD-based policies in the US. Notably, the disparities between the two countries could be attributed to the significantly higher organ donor numbers in the US as there was no significant improvement of waiting list mortality in the US after adjustment for donor number (OR: 1.01, 95% CI: 0.97 - 1.06). Similarly, survival after transplantation did not show significant improvement after adjustment for donation rates in the US (HR: 0.96, 95% CI: 0.90 - 1.01). In addition, a combined multivariable cox-proportional hazards regression model of the two countries showed a markedly reduced difference in patient survival after adjustment for donor number (unadjusted HR for survival in Germany compared to the US: 2.12, 95% CI: 2.04 - 2.20; adjusted HR: 1.44 (95%CI: 1.30 - 1.59).

Conclusion

MELD-based liver allocation demonstrates improved waiting list outcomes and post-transplant survival in the US with high donor numbers. Consequently, there is a need for a critical re-evaluation of liver allocation policies in countries with limited organ donation rates like Germany.

Lung in General

WS06-04

Analysis Of Perioperative Factors Leading To Postoperative Pulmonary Complications, Graft Injury And Increased Postoperative Mortality In Lung Transplantation

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Introduction

Postoperative complications such as pulmonary (PPC) and other organ complications are associated with increased morbidity and mortality after successful lung transplantation and have a detrimental effect on patient recovery.(1) The aim of this study was to investigate perioperative risk factors for in-hospital mortality and postoperative complications with a focus on PPC and graft injury in patients undergoing lung transplantation.

Methods

During the period from 2012 to 2022, a retrospective analysis of all consecutive patients aged >18 years undergoing lung transplantation at the University Hospital of Freiburg, Germany, was performed analysing the patient records of 173 patients as anonymised data sets. The study was approved by the Ethical Committee of the University Hospital of Freiburg (AZ 431/14). Informed consent was waived due to the retrospective character of this study.

Results

In the stepwise multivariate regression analysis, donor age >60 years (OR 1.85, 95% CI 1.27-2.81), intraoperative ECMO

(OR 2.4, 95% CI 1.7-3.3), transfusion of > 4 red blood cell concentrates (OR 3.1, 95% CI 1.82-5.1), mean pulmonary artery pressure > 30 mmHg at the end of surgery (OR 3.5, 95% CI 2-6.3), the occurrence of postoperative graft dysfunction (OR 4.1, 95% CI 2.8-5.9), PPCs (OR 2.1, 95% CI 1.7-2.6), sepsis (OR 4.5, 95% CI 2.8-7.3) and acute renal failure KDIGO 3 (OR 4.3, 95% CI 2.4-7.7) were associated with increased in hospital mortality, while COPD patients had a lower in-hospital mortality (1.6, 95% CI 1.4-1.9). The frequency and number of PPC correlated with postoperative mortality.

Conclusion

Clinical management and risk stratification focusing on the underlying, identified factors could help improve patients' outcome.

Reference

[1] Diamond JM, Arcasoy S, Kennedy CC, et al: Report of the International Society for Heart and Lung Transplantation Working Group on Primary Lung Graft Dysfunction, part II: Epidemiology, risk factors, and outcomes-A 2016 Consensus Group statement of the International Society for Heart and Lung Transplantation. J. Heart Lung Transplant. 36:1104–13, 2017

WS06-05

Soluble Immune Mediator Profiling Identifies Immunological Conditioning Of Ex Vivo Perfused Lungs Associated With The Severity Of Primary Graft Dysfunction (PGD)

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Introduction

Clinical lung preservation procedures have strong impact on post-transplant outcome. However, the physiological link between key post-transplant clinical parameters and immunological alterations, especially during ex vivo lung perfusion (EVLP) are still poorly defined.

Methods

Soluble immune mediators (SIM, n=103) i.e. cytokines/chemokines, growth, adhesion molecules were quantified in lung preservation solutions and in recipient plasma before (*pre*), after (*post*), 24h and 3wks post-LTx in EVLP (n=36) vs standard of care (SOC) (n=26) patient subgroups by Luminex-based multiplex assays and correlated to clinical parameters.

Results

SOC was associated with more unstable clinical dynamics and higher risks for PGD score 3. Despite generally higher levels of SIM in normothermic EVLP perfusates vs SOC preservation solutions, the ratios of pro- to anti-inflammatory SIM such as IFN-γ/IL-10, IL-33/IL-10, IL-6/IL-6R were significantly lower in EVLP, pointing to a reduction in pro-inflammatory milieu. Consistently, in recipient plasma, several pro-inflammatory SIM showed significantly lower levels (IL-6, GM-CSF, CXCL10) in EVLP recipients. Of note, the higher levels of these SIM in SOC recipients correlated with higher PGD scores. Also, SIM such as IL-6, IL-18, sCD40L, EGF, VEGF, and endoglin were correlated with cold ischemic time in SOC, indicating a potential triggering during cold ischemic/hypothermic conditions. In addition, uPA and VCAM-1 were identified as biomarkers that universally correlated to a higher PGD score and hypoxemia (low PiO_2/FiO_2 ratio) in both subgroups. Finally, we uncover a significant association of the patient's primary diagnosis with PGD severity, particularly in the case of PAH and sarcoidosis.

Conclusion

Our analysis identified a complex interplay between key clinical parameters such as PGD score, hypoxemia,

ischemic time, and the dynamic and levels of immune parameters as well as primary diagnoses. Considering these parameters during LTx may pave the way to improved therapeutic options and transplant outcomes.

WS06-06

Outcomes Of Intraoperative (not) Elective Extracorporeal Circulatory Support In Lung Transplantation For Pulmonary Fibrosis Three Years After Protocol Adjustment

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Introduction

Selected patients with pulmonary fibrosis undergoing lung transplantation may benefit from intraoperative elective extracorporeal membrane oxygenation (ECMO). Based on previous studies, our institution adjusted 2020 its ECMO protocol in these patients.

Methods

All Patients with pulmonary fibrosis undergoing LTx between 01/2012–12/2023 were included in this study. Patients were sub-divided into the period before and after protocol adjustment. Further, patients of both study periods were sub-divided into elective, not elective and no intraoperative ECMO support.

Results

Out of 119/427 patients transplanted since 2020, 73 (61%) required elective ECMO, 11 (9%) not elective ECMO and 35 (30%) underwent LTx without ECMO support. Before 2020, 308 patients with pulmonary fibrosis were transplanted (elective ECMO n=60 (19%); not elective ECMO n=31 (10%); no ECMO n=217 (70%)). Based on our protocol implementation, patients requiring elective ECMO showed pre-transplant increased pulmonary vascular resistance (PVR: median 3.9 vs. 2.5, p<0.001) and mean pulmonary arterial pressure(PAPmean: median 30 vs. 22, p<0.001) compared to patients without ECMO. Therefore, cut-off values in PAPmean (>26mmHg) and PVR (>3.07WU) are recommended to decide whether elective ECMO support is initiated. However, the initial pre-transplant clinical presentation of 11 patients appeared as no ECMO is required. Peri-transplant, not elective ECMO implantation was necessary. Compared to patients with no ECMO, an inferior donor organ quality assessed by donor age, smoking history and ventilation time was absent as well as differences in recipient characteristics. Assessing Primary Graft Dysfunction 72-hours post-transplant between elective (4.1% vs. 15.5%, p=0.025), not elective (0% vs. 36.7%, p=0.025) and no ECMO support (2.9% vs 12%, p=0.105) between study periods, a clear improvement can be shown. Similar, 1-year graft survival improved in elective (94.3% vs 81.7%), not elective (90.9% vs 71%) and no ECMO patients (91.4% vs. 90.7%), though not statistically significant.

Conclusion

Elective intraoperative ECMO support in selected patients with pulmonary fibrosis is reasonable due to increased PAP as well as PVR.

Immunology

WS07-05

Viro-Immunological Monitoring As A Predictor For Complicative Events In The First Year After Kidney Transplantation: The VIRENO Study

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Introduction
VIRENO is an interdisciplinary, multicenter study aiming to identify clinical and immunological parameters that predict major infectious and immunological adverse events after kidney transplantation (KTx), using a combination of biosamples and clinical outcome at five German Transplant Centers.

Methods
Viro-immunological monitoring, including anti-BK-polyomavirus IgG, anti-cytomegalovirus (CMV) IgG and T-cell reactivity and torque teno virus (TTV)-DNA load), was performed pre-KTx, 3 weeks and 6 months post-KTx. Clinical parameters were recorded baseline and during follow-up 3 weeks, 6 months and 12 months after transplantation, focusing on infection- and rejection-related endpoints. Three different univariate analysis were used for identifying features associated with the outcome: logistic regression (LR), correlation and LASSO. Variables showing a significant association to the different endpoints were selected for further model generation by random forest (RF) or LR. Next, models for prediction of infectious and rejection events were further optimized by model training, cross-validated and analyzed for their quality (area under the curve, AUC). The best infection model and the best rejection model were summarized to the VIRENO-score predicting adverse events after KTx.

Results
In total, 196 patients were followed up for one year after KTx and 113 infectious and 30 rejection events were recorded. The best model for predicting the infection endpoint consisted of a variable set of 13 variables including different HLA constellations in donor and recipient, baseline TTV-DNA load in plasma and CMV serostatus of donor and recipient (AUC 0.802). The best rejection model consisted of 10 different variables including CMV-IgM at baseline, the presence of underlying immunological diseases, preformed donor specific antibodies, and different HLA constellations (AUC 0.867). In addition, the combination of both scores (VIRENO-score) was suitable predicting both adverse events after transplantation (AUC 0.774).

Conclusion
The combination of viro-immunological and clinical parameters is a promising tool for predicting major adverse events after KTx.

Ethics

WS08-03

Longterm Clinical Outcome 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 about the long-term clinical course and risk after living kidney donation.

Methods
HeiKiDS (Heidelberg Kidney Donor Study) is a cohort study investigating the longterm outcome of living kidney donors (LKD) at the Heidelberg Transplantation Center.

Results
A total of 373 LKD were studied prospectively (41.3% male, age 53.4±10.3 years (25-77y). Most donors were between 45 and 64 years old (72.3%), with 18% younger than 45 years. 36.4% donated to spouses, 40.7% to children, and 2.6% to friends. Preemptive LKD was performed in 32.9%, ABO-incompatible LKD in 32.5% and immunized LKD in 11.8%. S-creatinine was 0.76±0.15 mg/dL (eGFR 97.6±12.3 mL/min/1.73 m^2). BMI was 26.1 ± 3.5 kg/m2 (17-39 kg/m^2), with 2.2% donor BMI >35 kg/m^2. 49.7% donors had a relevant medical history (31.9% hypertension, 14.3% thyroid disease, 7.4% impaired glucose tolerance, 4.3% hyperlipidemia, 5.4% cardiac diseases, 4.6% urological diseases). 34.3% took medication regularly.

The median follow-up was 6 years including 217 donors with at least 5 years of follow-up. Postoperative complications occurred in 11.3% e (mainly infections, wound healing disorders, hematomas). Renal function decreased significantly with a loss of glomerular fitlration rate of 32.6%, but stable function in the longterm. Two donors showed eGFR <30 ml/min/1.73 m^2 at last follow-up. No change in BMI, blood pressure and microalbuminuria after LKD was observed. Antihypertensive medication increased from 21.1% before LKD to 37.0% at last follow-up. The prevalence of hypertension was 45% at last follow-up. 3 donors died (esophageal cancer, glioblastoma, malignant melanoma; 3 to 6 years after donation), none of the donors received renal replacement therapy.

Conclusion
Around 50% of donors were people with previous illnesses. A 30% decline in renal function after LKD, but long-term stable renal function was confirmed. The prevalence of high blood pressure rose up to 45%. No serious complications directly related to LKD were observed. In order to ensure appropriate medical care, especially for donors with previous illnesses, regular follow-up examinations at the transplant center are necessary.

We thank all participating kidney donors and the HeiKiD staff.

Transplant Registry

WS10-01

Enhancing Transplantation Research: The Next Chapter For The German Transplantation Registry

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Introduction

The Gesundheitsforen Leipzig GmbH has received approval to operate the German Transplant Registry (Tx Registry) for an additional five years. Since its inception, the Tx Registry has integrated data from the German Organ Transplantation Foundation (DSO), Eurotransplant (ET), and the Institute for Quality Assurance and Transparency in Healthcare (IQTIG). According to §15a of the German Transplantation Act (TPG), the Tx Registry aims to enhance the data foundation for healthcare and research in transplantation medicine, promoting more transparency and quality. Previous research utilizing the registry's data has faced challenges due to the comprehensiveness of the dataset and data quality issues. Therefore, the Tx Registry will be enhanced in a 4 steps plan.

Methods

To improve data quality and usability, several measures are planned:

1. Tools for Users: Future provision of tools to facilitate data handling.
2. Data Model Adjustment: Creation of a core dataset to improve usability and increase international comparability.
3. Reduction of Redundancies: Minimization of redundancies arising from data exchanges between data providers before transmission to the Tx Registry.
4. Introduction of Data Standards: Long-term implementation of standards like HL7 FHIR to improve data quality and facilitate international data exchange.

Results

While the implementation and evaluation of these measures' success is still pending, the number of data exports could serve as a potential indicator of success.

Conclusion

The planned measures aim to significantly enhance data quality and the usability of the Tx Registry. By providing user tools and adjusting the data model, more efficient data utilization will be achieved enabling research that could result in updates to clinical guidelines and allocation rules. Reducing redundancies and introducing international data standards will further improve data quality and advance international data exchange and global research. The development of the Tx Registry is a crucial step towards improving the foundations for healthcare and research in transplantation medicine.

WS10-03

Antibiotics, Glucocorticoids And Catecholamines - A Pharmacotherapeutic Analysis Of The German National Transplant Registry Data From 2006-2016

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Introduction

Brain-dead organ donors receive comprehensive pharmacotherapy to preserve organ quality, affecting the recipient directly or indirectly. Data on this practice have been scarce in Eurotransplant (ET) countries. The German National Transplant Registry now provides such data and allows for structured analysis.

Methods

Standardized registry data from 2006-2016 (BED old data, V1.2.3) were assessed. Data on medication of 12,293 postmortem donors were provided by the German Organ Procurement Organization (DSO), documented by DSO coordinators based on hospital records from immediately before the diagnosis of brain death until organ retrieval. Medications were coded using the official Anatomical Therapeutic Chemical (ATC) clas-

sification for Germany (Version 2023). In this study, we assessed the prevalence of anti-infectives, catecholamines, and glucocorticoids.

Results

Complete medication documentation was available for a total of 12,293 donors (median age 54 years (Q25; Q75: 43; 67); 46.5% female). Between 1 and 24 substances were documented per donor (median 7 (Q25; Q75: 6; 10)). Among these, 8,542 (69.5%) donors received at least one anti-infective drug, of which the three most common substances were piperacillin with beta-lactamase inhibitors (ATC: J01CR05, n=2,307, 18.8%), ceftriaxone (J01DD04, n=1,944, 15.8%), and cefuroxime (J01DC02, n=1,086, 8.8%). Aminopenicillins (J01CA01, J01CA04, J01CR01, J01CR02) were prescribed in n=1,431 (11.6%). Catecholamines were given to n=10,693 (87.0%), with norepinephrine (C01CA03) in n=10,546 (85.8%), dobutamine (C01CA07) in 886 (7.2%), and dopamine (C01CA04) in n=218 (1.8%) as the most frequent. Glucocorticoids were given to n=6,768 (55.1%), including hydrocortisone (H02AB09, n=4,188, 34.1%), methylprednisolone (H02AB04, n=2,140, 17.4%), and prednisolone (H02AB06, n=615, 5.0%) as the most frequent.

Conclusion

The available German National Transplant Registry data provide first insights into a comprehensive picture of donor pharmacotherapy. Detailed documentation of antibiotics, catecholamines, and glucocorticoids were assessed, enabling future studies on the outcomes of these therapies in recipients.

WS10-04

The Effect Of Dopamine On Graft Failure After Kidney Transplantation – An Analysis Of Data From The German National Transplant Registry

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Introduction

Available data on dopamine use in brain-dead organ donors to improve kidney transplantation outcome are conflicting. Although the German Organ Procurement Organization recommends it, dopamine still has not become part of standard care in most German hospitals facilitating organ procurements.

Methods

The German National Transplant Registry included 16,155 isolated kidney transplantations from postmortem donors with available information regarding their medication and to recipients with no prior or subsequent transplantation of any organ registered at Eurotransplant (ET) from 2006 to 2016. Information on postoperative graft function, documented by the BQS Institute for Quality and Patient Safety (until 2009) and aQua (Institute for Applied Quality Improvement and Research in Health Care, since 2009), was available for 13,868 recipients.

Results

Donors for 287 (2.1%) recipients had been treated with dopamine prior to organ procurement. Postoperative kidney graft function was negated in 1,865 (13.4%) recipients. Dopamine use was associated with decreased risk of non-function (5.9%, n=17) compared to 13.6% (n=1848) in recipients of kidneys from donors without dopamine use (risk ratio 0.44, 95%CI (0.27; 0.69)). Restriction to 12,766 transplantable recipients (allo-PRA% 0-5) and further adjustment for recipient and donor age did not change the risk ratio (0.47 (0.29; 0.75)). Making use of incomplete data on postoperative dialysis (BQS, aQua, ET) and competing reasons for graft failure (ET), recipients with hyperacute rejection or vascular or ureteric operative problems were excluded. Additionally, recipients with reported non-function but no postoperative dialysis or with a functioning graft but with the need for postoperative dialysis or primary or permanent non-function were precluded from further analysis. In this sensitivity analysis, the adjusted risk ratio for dopamine vs. no use remained statistically significant (0.40 (0.17; 0.95)).

Conclusion

Overall, there seems to be a beneficial effect of dopamine regarding initial graft function after isolated kidney transplantation. The effect remained when adjusting for age and excluding recipients with questionable classification of graft function.

WS10-05

Graft Failure After Kidney Transplantation From Donors With Carbon Monoxide Poisoning – An Analysis Of Data From The German National Transplant Registry

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Introduction

It remains unknown whether death by carbon monoxide (CO) poisoning in organ donors can impact kidney transplantation outcomes, possibly by CO-induced permanent organ injury. While reports of successful solid organ transplantations from CO-poisoned donors, as well as preclinical studies suggesting beneficial effects, have been published, other reports demonstrating donor organ failure and early recipient death are also available. Therefore, a retrospective analysis of data from the German National Transplant Registry was conducted.

Methods

The registry included 12,296 postmortem donors of kidney transplantations with information on the cause of death, of whom 16 were diagnosed with CO-poisoning. All 32 concerned kidneys were procured, but only 30 transplantations were recorded by Eurotransplant (ET). Of these, 25 were isolated kidney transplantations to recipients with no prior or subsequent transplantation

registered at ET of any organ from 2006 to 2016. Information on postoperative graft function was available for n=17. We identified 9,758 isolated kidney transplantations from 6,444 donors without CO poisoning with a similar age range (8-70 years) and ICU care duration to organ recovery (1-11 days).

Results
Rescue allocations were more frequent in transplantations from donors with compared to those without CO-poisoning (24%; n=4 vs. 7.3%; p=0.03), whereas recipient age distribution was similar (mean 50.5 vs 52.5 years; p=0.56). Postoperative graft function was registered as impaired in 29% (n=5) vs. 13.1% of recipients (p=0.06). Sensitivity analyses by excluding recipients with potentially misclassified outcome strengthened the observed difference (25%; n=4 vs. 5.4%; p=0.009).

Conclusion
All kidneys from donors who died from CO-poisoning were successfully allocated and most were transplanted. In a subset with complete follow-up, we found a considerably higher incidence of graft non-function. The small sample size hinders evaluation of potential confounders, such as rescue allocation or other recipient or donor characteristics. Further analyses for kidney and other organ transplantations are warranted to evaluate whether transplantations from donors after CO poisoning are safe.

HTX - Congenital Vitia

WS12-07

Persisting Protein-Losing Enteropathy After Orthotopic Heart Transplantation In Failing Fontan

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Introduction
Protein-losing enteropathy in failing Fontan circulation carries a high risk of complications during and after heart transplantation. Previous surgery, liver dysfunction, coagulopathies, and malnutrition are possible concomitant and consequential damages of "Fontan circulation" and place high demands on perioperative care. Due to the rarity of such cases, guidelines and recommendations are limited. Deciding on the right time for transplantation seems to be essential.

Methods
The 20-year-old patient with Fontan circulation after double inlet left ventricle (DILV) and dextro-transposition of the great arteries (d-TGA) suffers from secondary protein-losing enteropathy (PLE) and pubertas tarda (1.52 m / 38 kg). The patient underwent orthotopic bicaval heart transplantation 16 years after total cavopulmonary connection (TCPC).

Results
The postoperative course was protracted, and renal insufficiency requiring dialysis persisted. Serial ultrasound follow-ups showed good left ventricular and right ventricular function (left ventricular ejection fraction 64%, right ventricular fractional area change > 60%). Enteral protein loss did not improve significantly even six months after transplantation, so transhepatic lymphosclerosis of the portal veins was performed in a specialized clinic. In the case of persistent portal hypertension with consecutive ascites, transjugular intrahepatic portosystemic shunt (TIPS) was performed 6 months post-transplant without complications. Albumin and pentaglobin are still being substituted, with total protein and albumin at a stable low level.

Conclusion
This case report shows a protracted postoperative course after heart transplantation for Fontan failure with PLE. Heart transplantation remains the gold standard of therapy after Fontan failure, although the sequelae of long-term Fontan circulation pose challenges in peri- and postoperative management. This case underlines the need for an interdisciplinary and specialized approach in a highly complex disease entity.

We thank the entire team for the interdisciplinary collaboration in this complex case.

References

[1] Konstantinov IE, Schulz A, Buratto E., 2022, 'Heart transplantation after Fontan operation.', JTCVS Tech. 2022 Jun; 13: 182–191, doi: 10.1016/j.xjtc.2022.01.020.

[2] Barracano R, Merola A, Fusco F, Scognamiglio G, Sarubbi B. 2022. 'Protein-losing enteropathy in Fontan circulation: Pathophysiology, outcome and treatment options of a complex condition.' Int J Cardiol Congenit Hear Dis, 7:100322 DOI: https://doi.org/10.1016/j.ijcchd.2022.100322.

[3] Schumacher KR, Yu S, Butts R, Castleberry C, Chen S, Edens E, Godown J, Johnson J, Kemna M, Lin K, Lowery R, Simpson K, West S, Wilmot I, Gossett JG. 2019. 'Fontan-associated protein-losing enteropathy and post-heart transplant outcomes: A multicenter study.' J Hear Lung Transplant, 38(1):17–25 DOI: https://doi.org/10.1016/j.healun.2018.09.024.

Preconditioning

WS13-04

The Impact Of Preoperative Body Composition And Fat-To-Muscle Ratio On Graft- And Patient Survival In Human Kidney Transplantation

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Introduction

Preoperative assessment of body composition (BC) has emerged as a useful tool in patients undergoing organ transplantation. While body-mass index (BMI) and obesity are well-established markers for poor clinical outcome, the relation of fat tissue and muscle mass (fat-to-muscle ratio-FMR) as a preoperatively available prognostic marker in kidney transplantation (KT) remains to be determined.

Methods

473 consecutive KT recipients [n=294 (62%) living-donor, n=179 (38%) deceased-donor] from a prospective database (2010-2020) with completed computed tomography (CT) within one year before KT were analyzed retrospectively. CT-based lumbar skeletal muscle area (SMA), total adipose tissue area (TATA) and mean muscle attenuation were calculated using a segmentation tool (3DSlicer). BC parameters (sarcopenia, visceral obesity, myosteatosis) were identified using predefined cutoff values. The FMR was used to estimate fat and muscle distribution using the ratio of SMA and TATA normalized for recipient's height. Parametric- and non-parametric tests, uni- and multivariable logistic regression were used to determine the association of BC with clinical outcome.

Results

The cutoff values for FMR resulted in good stratification of patients into low- and high-risk groups in terms of perioperative morbidity (Clavien-Dindo-CD/Comprehensive Complication Index-CCI). High FMR was an independent risk factor in uni- and multivariable Cox regression analysis for graft- and patient survival. Patients with higher FMR had significantly more severe complications (Clavien-Dindo≥3b: 76[23%] vs. 59[40%];p<0.001) and cumulative complications after 90 days (CCI: 32±57 vs. 20±36;p<0.001). Increased FMR was associated with an approximately 3-fold increased risk for recipients' death (HR 2.84, CI-95%: 1.2-6.5;p=0.014), decreased graft- (43 vs. 34 months; adjusted p=0.017) and patient-survival (45 vs. 36 months; adjusted p=0.017), respectively.

Conclusion

The assessment of FMR as independent prognostic marker influencing perioperative outcomes, graft- and patient survival underline the clinical significance of preoperative BC assessment in human KT.

WS13-05

Strategies On Nutritional Assessment And Supplementation In The Liver Transplant Candidates

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Introduction

Malnutrition is a frequent complication in patients with cirrhosis and liver transplant (LT) candidates [1]. It is highly related to sarcopenia and frailty, and their implications in morbidity and mortality go beyond the waiting list period throughout the post-LT. However, there are no specific interventions defined by guidelines, including the current German guideline, regarding the kind or the timing of the nutritional intervention to improve LT outcomes. The main limitations of the previous studies are the retrospective nature of some of them, the variety of interventions and the heterogeneous measurement of the intervention effect, which makes comparisons between studies difficult.

Methods

In a single-center, single-arm, non-randomized clinical trial we investigated the effect and feasibility of nutritional assessment [1] (nutritionist, RFH-SGA, LFI, SF-36, MFI) in inpatient LT evaluation and home-based intervention (nutritional plan, nutrition guide [2], nutritional-APP).

Results

Over 50% of the LT candidates had manifest malnutrition and the resulting consequences. With the home-based intervention, an improvement in nutritional and muscle status could be achieved.

Conclusion

In contrast to older studies, a significant improvement in nutritional status was achieved using standardized screening procedures and modern intervention strategies. The general recommendation for patients awaiting LT is that general nutrition should be ensured as early as possible. This should be preceded by a meaningful evaluation; standardized tools will benefit research purposes and the comparability and repeatability of the studies. We recommend that each center chooses their best center-adapted strategy based on their own resources, encouraging to cover a minimum nutritional status evaluation with a basic dietary intake collection (lays the grounds to suggest changes), and muscle or frailty evaluation (LFI preferred).

References

[1] Dobbermann, H., Guenther, R., Marquardt, J. U. Aktuel Ernährungsmed 2021; 46: 109–126

[2] Guenther, R., Guenther. C. Ernährungsratgeber bei Leberzirrhose 2020 https://www.uksh.de/uksh_media/Dateien_Kliniken_Institute/Kiel+Campuszentrum/Innere1_KI/Dokumente/Hepatologie/Brosch%C3%BCre_Ern%C3%A4hrung_bei_Leberzirrhose.pdf

Management of Complications After Liver Transplantation

WS14-05

How Are The 100 Years Old Transplanted Livers Doing?

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Introduction

The accepted donor age is increasing significantly due to organ shortage, especially in Germany. The short term outcome of elderly donor grafts are well studies.

However, the question about the graft function 10-20 years after transplantation is not sufficiently answered. The aim of this study was to evaluate the liver function of donor grafts ≥ 100 years.

Methods
Between 01/2007 to 12/2020 there were 52 liver transplantations with donor age of ≥ 80 years (23 female (44%)). Out of these, all patients who are still alive and have a liver graft age of ≥100 were identified. Pre-, intra and postoperative data and follow-up data were retrospectively analyzed.

Results
There were nine patients (17.3%) with liver graft age of ≥100 years (6 female (66.7%)). At the time of transplantation, mean age was 57.7 years, mean lab-MELD was 19. The mean cold ischemic time was 5h 15 min., none of the liver grafts had significant macrovesicular steatosis in the histopathological examination. There were no intraoperative complication; three patients received intraoperative blood transfusion (two units). Mean duration of surgery was 230.5 minutes; mean warm ischemic time was 31.5 minutes. The mean ICU stay was 13 day. and mean hospital stay was 33.8 days. Major postoperative complications were seen in five patients, which could be treated successfully. After mean follow-up of 158.1 months all patients have still excellent liver function with normal liver blood tests.

Conclusion
Based on the data, we can assume that donor age is not a significant factor for the liver function in long-term. Factors such as steatosis of the donor graft are likely to be more significant for the long-term graft function.

Infectology

WS15-02

Etiological Shifts In Infections Beyond The First Year After Transplantation - Results Of The DZIF Kidney Transplant Cohort

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Introduction
Our aim was to provide a detailed insight into the frequency and etiology of infections beyond the first year after renal transplantation.

Methods
All proven and probable infections occurring within the first three years after transplantation were assessed in the adult kidney transplant cohort of the German Center of Infection Research (DZIF) enrolled from 04/2014 to 07/2020.

Results
815 renal transplant recipients (65.4% male, mean age 51±14 years) were examined. A total of 1892 infections were recorded, with 68.2% occurring in the first year, 18.9% in the second, and 12.9% in the third year. Bacterial infections predominated throughout. In the second year,

the cumulative incidence rates were 16.4% [14.0;19.3] for bacterial, 9.4% [7.5;11.7] for viral, and 2.9% [1.9;4.4] for fungal infections. In the third year, rates decreased to 12.9% [10.7;15.6], 10.1% [8.2;12.5], and 0.2% [0.1;1.1], respectively.

Notably, a significant shift in bacterial etiology from gram-positive strains to gram-negative strains was observed, mainly due to declining proportions of Enterococcus isolates and increasing proportions of E. coli and Pseudomonas aeruginosa isolates. 4-MRGN-isolates among all Pseudomonas aeruginosa isolates increased to 37.3% in the third year. The viral etiology was consistently dominated by CMV and BKV, with proportions decreasing over time (85.3% to 42.3%) while the proportions of HSV-1, VZV, and EBV increased (8.2% to 25.0%). Candida albicans and non albicans spp. were predominant among fungal pathogens in all observed time periods (mean: 51.8% and 31.5%). Pneumocystis jirovecii was observed within the first (10.3%) and second year (15.8%) and Aspergillus fumigatus only in the first year (8.6%), reaching its peak between months 1 and 6 (16.0%).

Conclusion

Our results showed a significant decrease in posttransplant infections beyond the first year, as well as a shift toward gram-negative bacteria, multidrug-resistant strains, and certain herpesviruses. These findings highlight the dynamic nature of infection after kidney transplantation and call for careful monitoring, and tailored antimicrobial strategies, even in the longterm after transplantation.

WS15-03

Infections During The Early Inpatient Period Following Transplantation - Insights From A Large Renal Transplant Cohort

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Introduction

Our aim was to provide insights into the infectious episodes and antimicrobial management during the inpatient period after transplantation.

Methods

We analyzed all infectious events during the initial inpatient period in adult participants of the Transplant Cohort of the German Center for Infection Research (DZIF), Heidelberg site, between 11/2012 and 03/2024.

Results

Among 604 recipients (63.3% male, mean age 49±14 years), 58 confirmed infections occurred in 48 (8.0%) recipients within the initial inpatient period. Median time of onset was 12 days (IQR 9-18). Bacterial infections comprised 84.6% of cases, dominated by gram-positive bacteria (66.7%), notably Enterococcus spp., Staphylococcus spp., and Clostridium difficile. Antimicrobial resistance was reported in 14.3% of bacterial infections, primarily due to VRE, isolated in 37.3% of Enterococcus spp. infections. Viral infections (13.8%) were predominated by respiratory viruses (90.0%), mainly RSV and Influenza. Fungal infections were rare (1.7%), with only one case of Candida glabrata fungemia reported. Primary infection types included urinary tract- (42.1%), respiratory tract- (17.5%) and bloodstream infections (12.3%). Except for one case of HSV-1 pneumonia, opportunistic infections were absent. Moreover, there were 18 cases treated with antibiotics, where either no infectious focus could be identified despite clinical suspicion or where pathogens were detected without concurrent infectious symptoms. Overall, the most frequently prescribed antibiotics included Piperacillin/Tazobactam (26.3%), Vancomycin (20.2%) and Meropenem/Imipenem (15.2%), with 47.5% of recipients receiving multiple agents. Notably, at least 67.3% of antibiotic-treated patients experienced an additional bacterial infection within the first year, requiring rehospitalization after a median of 37 days (IQR 27-57) following the initial infectious event.

Conclusion

The special etiology of early infections, coupled with the extensive use of broad-spectrum antibiotics and the high incidence of subsequent infections, underscores

the need for refining antimicrobial strategies during the inpatient period after kidney transplantation.

WS15-04

Herpesviruses Beyond Cytomegalovirus: Short And Long-Term Incidences And Valganciclovir Prophylaxis Efficacy In A Large Cohort Of Renal Transplant Recipients

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Introduction
Kidney transplant recipients are at high risk of herpesvirus infections. Despite extensive research on CMV infections after transplantation, long-term data on the incidence of other herpesviruses are lacking, particularly in relation to valganciclovir, which is primarily used for CMV prophylaxis.

Methods
As part of the Transplant Cohort Study led by the German Center for Infectious Diseases (DZIF), we examined all herpesvirus infections beyond CMV in adult participants who underwent kidney transplantation at our center in Heidelberg between 11/2012 and 03/2024.

Results
604 recipients were enrolled (63.3% male, mean age 49±14 years). Median follow-up was 5 years. 62.4% received CMV prophylaxis with Valganciclovir for at least 3 months. The incidence-rate of other herpesviruses was 3.7% [2.4;5.6] in the first year, rising to 10.5% [7.5;14.8] over the entire follow-up period. Among patients receiving prophylaxis, incidence rate was 8.8% [5.4;14.6], compared to 12.9% [8.5;19.7] in those without prophylaxis (p=0.007). Notably, the most significant difference was observed in the initial year (0.9% [0.3;2.7] vs. 8.4% [5.4;13.0], p<0.001), diminishing over time. VZV affected 6.2% [4.2;9.2] of recipients presenting as herpes zoster, while HSV-1 occurred in 4.0% [2.2;7.3] of recipients, comprising 7 cases of HSV-1 pneumonia. Additionally, one case of EBV-associated post-transplant lymphoproliferative disorder (PTLD) was diagnosed 218 days post transplantation (D-EBV+/R-EBV+; immunosuppression: IL2-ab, CsA, MPA, steroids). Median onset for VZV and HSV-1 infection was 471 days (144-1043) and 153 days (42-298), respectively. Recipients without prophylaxis showed shorter onset times: 152 days (51-238) for VZV and 72 days (42-120) for HSV-1.

Conclusion
Kidney transplant recipients without valganciclovir prophylaxis are at significant risk of HSV and VZV infection in the first year after transplantation. However, despite initial effectiveness, susceptibility to these infections persists in the long term, unlike other post-transplant infection risks.

WS15-05

Vigilance Data In Organ Donation And Solid Organ Transplantation In Germany: Donor-Derived Infections In Germany From 2016-2023

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Introduction

In many cases, organ transplantation is still the only therapeutic option that can sustainably improve the life expectancy and quality of life of patients with terminal organ failure. Despite continuous improvements in donor and organ assessment, there remains a residual risk of transmission of an infection, tumor or other disease from the donor to one or more recipients. The careful analysis, reporting and managing of donor-derived diseases (DDD) through a vigilance and surveillance system (V&S) is mandatory in many countries. Here we report on the subgroup of suspected and proven/probable donor-derived infections (DDI) in Germany over a period of 8 years from 2016-2023.

Methods

All incoming serious adverse event (SAE) and serious adverse reaction (SAR) reports from January 1, 2016 to December 31, 2023 were evaluated for suspected DDI. The analysis of the degree of imputability followed the definition of the US Disease Transmission Advisory Committee (DTAC). Only probable and proven cases according to the classification of the DTAC were defined as DDI.

Results

During the study period 9771 donors in Germany donated post-mortem organs to 27919 recipients. In the same period 612 SAE/SAR cases were reported, 377 (62%) involved infections. In 41 cases affecting a total of 58 recipients the infection was classified as a proven/probable DDI. 7 of the 58 recipients (12%) died. Most of the infections were bacterial (182/377, 48%), followed by fungal (135/377, 36 %), viral (55/377, 15 %) and parasitic (5/377, 1 %) infections. In case of a bacterial DDI, no recipient died, but an organ loss occurred in six recipients. In case of a fungal or viral infection, 19 % (3/16) and 21 % (3/14) of the affected recipients died, respectively.

Conclusion

DDI are rare in solid organ transplantation (58/27919, 0,21 %), but when they do occur, they are associated with high morbidity and mortality in the affected recipients [1]. Careful and detailed donor evaluation and a reliable vigilance and surveillance system can help improving recipient safety [2].

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

References

[1] Kaul DR, Vece G, Blumberg E, et al. Ten years of donor-derived disease: A report of the disease transmission advisory committee. *Am J Transplant*. 2021;21(2):689-702. doi:10.1111/ajt.161711.

[2] Bahakel HK, Pellet Madan R, Danziger-Isakov L. Approach to suspected donor-derived infections. *Front Pediatr*. 2023;11:1265023. Published 2023 Oct 4. doi:10.3389/fped.2023.1265023

Kidney - Transplantation of Highly Immunizied Patients

WS17-03

Usefulness Of Different Crossmatch Methods For Risk Stratification Prior To Living Donor Kidney Transplantation In Patients With Preformed Donor-Specific Antibodies

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Introduction

Preformed donor-specific HLA antibodies (DSA) are a well-known risk factor in kidney transplantation. There is still considerable debate, however, about the optimal risk stratification among patients with preformed DSA. Additionally, data on the prognostic value of different crossmatch assays in DSA-positive patients is scarce.

Methods

DSA-positive living kidney transplant recipients were selected from a multi-center study examining 4233 consecutive renal transplants. Additional seven patients from two further centres were included. Flow cytometric crossmatches (FXM) as well as Luminex-based crossmatches (LXM) and virtual crossmatches based on C1q- and C3d-binding antibodies (C1qXM, C3dXM) were performed retrospectively using pretransplant sera and lymphocytes isolated from fresh samples, which could be obtained from 44 donor and recipient pairs from 12 centres. Clinical

outcome data and the control group without DSA were compiled from the previous study, and supplemented by data on ten-year death-censored graft survival (10yGS).

Results

Between 19% (C3dXM) and 46% (FXM) of crossmatches were positive. Crossmatch-positive patients showed high incidences of ABMR within six months (up to 60% in B-cell FXM+ patients). The incidence of ABMR in crossmatch-negative patients ranged between 5% (FXM-) and 13% (C1qXM-). 10yGS was significantly impaired in patients with positive T-cell FXM and total FXM compared to both patients without DSA and to DSA-positive patients with negative FXM.

Conclusion

Especially FXM are useful for risk stratification, as the outcome of DSA-positive FXM- patients is similar to DSA-negative patients, while FXM+ patients have both more ABMR and decreased 10yGS. Due to their lower sensitivity, the significance of LXM, C1qXM and C3dXM would have to be examined in patients with stronger DSA.

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WS17-04

Kidney Transplantation in Highly Sensitized Patients via Eurotransplant's Acceptable Mismatch Program: A Retrospective Analysis of Long-Term Outcome, Impact of Induction Therapy and HLA Epitope Matching

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Introduction

Eurotransplant's Acceptable Mismatch (AM) program aims to expedite kidney transplants for highly sensitized patients. However, long-term clinical and immunological effects, including graft survival and development of *de novo* donor specific antibodies (dnDSA), remain under investigation. Optimal induction therapy for varying immunological risks and the impact of specific human leukocyte antigen (HLA) epitope matching on de novo DSA formation are unclear.

Methods

This retrospective, monocentric study analyzed 94 AM program kidney transplant recipients (transplanted between 2000-2019) and compared to control groups of non- (PRA 0-5%) and intermediate- (PRA 6-84%) sensitized patients that were transplanted through Eurotransplant Kidney Allocation System.

Results

Ten-year overall graft survival estimates were similar for non-sensitized and AM cohorts, while intermediate-sensitized patients showed a significant disadvantage. Antibody-mediated rejection rates were significantly lower in the non-sensitized group. Ten-year estimated dnDSA incidence was also lower in the non-sensitization group compared to AM, with no difference between AM and intermediately sensitized cohorts. In the intermediate group, the induction with interleukin-2 receptor antagonist (IL2RA) was associated with longer overall, and patient survival compared to depleting agents (ATG/OKT3). Broad HLA-A, -B, -DR mismatches and epitope mismatches were predictive for dnDSA formation in both the entire cohort and the AM subgroup.

Conclusion

The AM program's efforts are justified for timely transplants with acceptable risk profile and non-inferior outcomes. IL2RA induction appears superior for intermediate-sensitized patients compared to ATG/OKT3, without compromising rejection or dnDSA formation. *In silico* epitope matching might further reduce dnDSA risk, especially in high-risk AM patients.

Surgical Challenges in Transplant Surgery

WS18-03

Results Of More Than 50 Consecutive Laparoscopic Cystnephrectomies For Autosomal Dominant Polycystic Kidney Disease

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a common hereditary disorder and accounts for 5-10% of all cases of kidney failure. Nephrectomy is performed in up to 20 % of the patients due to compression symptoms, complications such as bleeding or infection or in preparation for kidney transplantation. The standard operating procedure for nephrectomy of large cystic kidneys is the open approach. We previously introduced the laparoscopic approach for those patients and now report the results of more than 50 consecutive cases.

Methods

All laparoscopic cystnephrectomies were performed at the surgical department of the Cologne University hospital between 08/ 2021 and 04/2024. Patients were placed in a lateral position with the ipsilateral side up and a 30° backward inclination. After installation of the capnoperitoneum the colon was mobilized and the ureter was localized and clipped. Hereafter, largest cysts were disrupted to minimize kidney volume followed by localization of the vascular pedicle which was subsequently dissected with a vascular stapler. After completion of mobilisation the kidney was excavated through a suprapubic incision after fragmentation of the kidney in a large recovery bag.

Results

52 consecutive patients underwent laparoscopic cystnephrectomy. Indications for surgery were preparation for transplantation in 32% (n=17), renal complications such as infection (27%; n=14) and bleeding (3%; n=2), compression symptoms (34%, n=18) and suspected malignancy (2%; n=1). Mean age of patients was 54 (± 9) years. Mean weight of cystic kidneys were 1715 g (± 1241 g). None of the patients needed conversion to open surgery. 25% (n=13) had Clavien-Dindo II complications such as iv antibiotics or blood transfusion, one patient had Grade III complication and no patients had higher grades of complications. The mean hospital stay was 12 days (± 7 days)

Conclusion

In our patient cohort, laparoscopic cystnephrectomy has shown itself to be a safe procedure. Even for cystic kidneys with relatively high weight over 1500g its complication rate is low. Therefore the laparoscopic approach for cystnephrectomy is our new standard approach for those patients.

Psychology / Psychosomatics

WS19-04

Qualitative Case-By-Case Analysis Of Nursing Patient Counselling For Organ Transplant Recipients

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Introduction

The organ transplant recipients are not considered cured, but chronically ill after the transplant, in a new, unfamiliar life situation, accompanied by many changes, due to the necessary lifelong use of immunosuppressive drugs [1,2,4]. In this context, patient education not only provides vital information, has a high impact on quality of life and adherence, but is a fundamental right, anchored in the Nursing Professions Reform Act. Due to the extensive changes, that affects all areas of life, effective communication, basic pedagogical knowledge and time are needed for education [3]. The aim was to evaluate the practice of patient education at four German transplant centers, to explore best practise models as well as problems & obstacles.

Methods

The present qualitative case-by-case analysis of nursing patient counselling at four German transplant centres was carried out as part of a bachelor thesis on the basis of expert interviews with both transplant nurses and nursing educators.

Results

There is a great need for advice, because many effects of immunosuppression on everyday life are unknown to organ transplant recipients.

Obstacles: nursing advice is not structurally anchored in everyday care and so at risk of failure. Language barriers prevent the transfer & absorption of information. Foreign-language organ transplant recipients are therefore structurally disadvantaged.

Regardless of the effect of counseling on adherence of organ recipients, patients have a right to evidenced-based counseling [3].

Conclusion

germanwide quantitative, questionnaire-based survey of care counselling at german transplant centres is needed to proof the present analysis. It is neccessary to provide evidencebased oral, visual & written information for foreign-language patients equal to the counselling for german speeking patients, to overcome the disadvantage of foreign-language patients..Structural anchoring of counselling, as well as uniform transfer of information is necessary to provide continuity of counselling and fullfill a patients right.

Stefanie Blumrich UKE Hamburg Eppendorf, Daniel Flenje, Monika Golebiowska MH Hannover, Sandra Köhler Universitätsklinik Köln, Jürgen Brakhage HDZ Bad Oeyenhausen

References

[1] Morrissey, P. E., Flynn, M. L. & Lin, S. (2007). Medication non compliance and its Implications in Transplant Recipients. Drugs, 67(10), 1463–1481.

[2] Fishman, J. A. (2007). Infection in Solid-Organ Transplant Recipients. The New England Journal of Medicine, 2601–2614.

[3] Sonntag, K., Reibnitz, C. von & Strackbein, D. (2017). Die Rolle der Beratung in der Pflege: Die Bedeutung der Beratung in den nationalen Expertenstandards für die Pflege. In C. von Reibnitz, K. Sonntag & D. Strackbein (Hrsg.), Patientenorientierte Beratung in der Pflege: Leitfäden und Beispiele. Springer.

[4] Schierhorn, M. & Segmüller, T. (2023). Patientenedukation als Aufgabe der Gesundheitsfachberufe. In I. Darmann-Finck & K.-H. Sahmel (Hrsg.), Pädagogik im Gesundheitswesen (S. 578–609). Springer.

WS19-07

Prevalence And Predictors Of Donor And Donation Images (DDI) In Patients After Heart Transplantation

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Introduction
Recovery as well as overall clinical outcomes following organ transplantation may be negatively influenced by psychological distress. Limited, mostly singular reports from organ recipients indicate that the upcoming thoughts and feelings related to the donor and/or the transplanted organ itself (so-called Donor and Donation Images; DDI) may be a source of psychological distress; however, our knowledge of DDI is limited. The present quantitative study is the first and largest study so far allowing for the development of a taxonomy of the phenomenon of DDI in heart transplantation (HTX).

Methods
We conducted a survey among adult patients who had undergone HTX at a German transplant center (N=1023).

Results
A total of 416 people participated to the survey. The prevalence of DDI was very high (91%). We found DDI to occur intermittently and often in close temporal proximity to the transplantation procedure (both before and after HTX). Psychological distress predicted the occurrence of DDI before and after HTX. Almost all emotions experienced and reported pre-HTX were associated with higher odds of pre-HTX DDI.

Conclusion
Pre-HTX DDI may be a side phenomenon of overall emotional activation. Due to the involvement of emotions associated with uncertainty and low personal/high situational control, DDI may be a part of coping. Some patients reported avoiding DDI suggesting that, in some cases, they might also represent a stressor. Future studies shall further investigate the effects of DDI including the impact on transplant outcome.

Young Transplantation Medicine Working Group

Y02-01

Impact Of Alloimunization Following Blood Transfusions Post-Renal Transplantation On Allograft Function And Occurrence Of ABMR

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Introduction

The administration of blood transfusions in organ recipients is a controversial subject. The potential risk of alloimmunization and hence potential risks for future transplantations and loss of allograft function seems to be obvious [1-3]. Nevertheless, the significance of post-transplant blood transfusions on alloantibody formation and the associated risk of chronic antibody-mediated rejection (ABMR) and impact on long-term renal allograft function remains unclear [4].

Methods

All renal transplant recipients transplanted at the Cologne Transplant Center between 2015 and 2019 were included. A retrospective analysis of HLA antibody formation after blood transfusion was performed. Donor and recipient HLA antibody typing was performed using Luminex®. The occurrence of any new antibody formation after transfusion was analyzed according to the occurrence of donor-specific (DSA), transfusion-specific (TSA) and both donor- and transfusion-specific antibodies (TSA_{DSA+}).

Results

Between 2015 and 2019, 287 patients underwent kidney transplantation at the Cologne Transplant Center. 61 (21%) patients had no Luminex® - HLA antibody screening post-transplant available, so that 226 patients were ultimately included in the analysis. 34,5% (n=99) patients received blood transfusions post-renal transplantation. 35% (n=36) of the transfused patients developed newly emerged HLA antibodies after transfusion. 13% (n=13) patients who received blood transfusions developed newly emerged donor-specific antibodies. Further analysis on the HLA-typing of the blood donors will reveal the amount of TSA and TSA_{DSA+} in this cohort as well as the impact of the newly emerged HLA antibodies on allograft function and occurrence of ABMR.

Conclusion

A significant proportion of transfused patients develop newly emerged HLA antibodies and/or donor-specific antibodies. ABMR is the leading cause of renal allograft failure, therefore the development of donor-specific antibodies post-transplantation must be avoided at all costs. We aim to perform further analysis in our patient population to prove or disprove the impact of newly emerged donor-specific and transfusion-and donor-specific antibodies on renal allograft outcome.

References

[1] J. C. Scornik and H. U. Meier-Kriesche, "Blood transfusions in organ transplant patients: mechanisms of sensitization and implications for prevention," *Am J Transplant*, vol. 11, no. 9, pp. 1785–1791, Sep. 2011, doi: 10.1111/J.1600-6143.2011.03705.X

[2] J. Aalten *et al.*, "Pre-kidney-transplant blood transfusions do not improve transplantation outcome: a Dutch national study," *Nephrol Dial Transplant*, vol. 24, no. 8, pp. 2559–2566, Aug. 2009, doi: 10.1093/NDT/GFP233

[3] G. S. Balasubramaniam, M. Morris, A. Gupta, I. R. Mesa, R. Thuraisingham, and N. Ashman, "Allosensitization rate of male patients awaiting first kidney grafts after leuko-depleted blood transfusion," *Transplantation*, vol. 93, no. 4, pp. 418–422, Feb. 2012, doi: 10.1097/TP.0B013E3182419864

[4] S. Hassan *et al.*, "Shared alloimmune responses against blood and transplant donors result in adverse clinical outcomes following blood transfusion post-renal transplantation," *Am J Transplant*, vol. 19, no. 6, pp. 1720–1729, Jun. 2019, doi: 10.1111/AJT.15233

Y02-02

Improving The Accuracy And Efficacy Of Organ Allocation Through Radiological Quantification For Liver Transplant Recipients

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Introduction

Large-for-Size Syndrome (LSS) is a rare but serious complication post-liver transplantation, characterized by the inability to close the fascia, early graft dysfunction, re-transplantation, or death. Discarding organs due to donor-recipient size mismatch (DRSM) prevents LSS but

increases waiting times and leads to the refusal of potentially transplantable organs. We propose that implementing effective risk stratification will increases acceptance rates without raising the incidence of LSS. This comprehensive approach aims to optimize transplant outcomes and improve overall liver transplant management.

Methods

Liver-only offers for patients undergoing liver transplantation at the University Hospital Münster between 01/2019 and 12/2023 were retrospectively analyzed. Morphological measurements were obtained from CT scans conducted within six months before transplantation. The longest right anteroposterior vertical distance between the anterior and posterior ribs (RAP) was measured. Estimated graft weight was determined using the donor's body surface area with the Mosteller formula[1,2]. The graft weight/recipient RAP ratio was then calculated. The primary outcome was the time to transplant.

Results

Out of 1,032 liver offers, 24% were rejected due to DRSM, with the majority being allocated to female recipients. A total of 64 patients were identified for which previous offers were declined due to DRSM but then successfully transplanted afterwards. On average, more organ offers were rejected for women than for men (3 vs. 2; p= 0.09). Median graft weight/recipient RAP ratio was 94 g/cm. Using the graft weight/recipient RAP ratio, 48% of declined organ offers would have been deemed suitable. This could have reduced the median time to transplant from 130 to 83 days, though the difference is not statistically significant (p=0.312).

Conclusion

Establishing radiological quantification for liver transplant recipients could improve the accuracy and efficacy of organ allocation. Incorporating these measurements into waiting list protocols will standardize the assessment process and enhance decision-making.

References

[1] Yoshizumi T, Gondolesi GE, Bodian CA, Jeon H, Schwartz ME, Fishbein TM, Miller CM, Emre S. A simple new formula to assess liver weight. Transplant Proc. 2003 Jun;35(4):1415-20. doi: 10.1016/s0041-1345(03)00482-2. PMID: 12826175.

[2] Mosteller RD. Simplified calculation of body-surface area. N Engl J Med. 1987 Oct 22;317(17):1098. doi: 10.1056/NEJM198710223171717. PMID: 3657876.

Y02-03

Unraveling Interindividual Differences And Functional Consequences Of Gut Microbial Metabolism Of Immunosuppressive Drugs

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Introduction

A major challenge in kidney transplantation (KT) is the large interpatient variability in the pharmacokinetics of immunosuppressants. We aim to provide a comprehensive understanding of the interindividual differences, functional consequences and underlying mechanisms of gut microbial metabolism of immunosuppressants.

Methods

We studied 25 drugs commonly used in KT, including 16 immunosuppressants, for their metabolism by 38 different human-derived gut microbial communities, including 10 from kidney transplant recipients, and 45 gut bacterial species. Drug degradation was assessed by liquid chromatography coupled to mass spectrometry-based metabolomics. The influence of microbial drug metabolism on enteric absorption was measured by assessing transport rates of drugs and

drug metabolites across a gut epithelial monolayer. Molecular mechanisms of gut microbial metabolism were evaluated by a gain-of-function genetic screen. Random forest-based machine learning models were used to predict drug degradation in the tested microbial communities.

Results

We revealed significant inter-individual and drug-specific differences in the metabolism of immunosuppressants. 15 of 16 immunosuppressants tested were metabolized by at least one microbial community, and specific species were identified as potent metabolizers. Our study reveals the functional impact of microbial metabolism on key immunosuppressants, including inactivation of tacrolimus, activation and potential increase in toxicity of mycophenolate mofetil (MMF), and increased epithelial permeability of the microbial metabolite of methylprednisolone compared to the parent drug. In addition, we identified the bacterial enzyme responsible for MMF activation. Abundance characteristics of the prevalent species predicted the biotransformation of some drugs well, while for others, experimental information on bacterial genes and enzyme protein structures led to better predictions.

Conclusion

Our research highlights the potential of gut microbiome characteristics to explain interindividual variability in metabolism of immunosuppressive drugs and sets the stage for clinical trials to identify microbiome-encoded signatures predictive of drug metabolism in KT.

Y02-04

Safety Of Dapagliflozin Treatment In Chronic Kidney Disease After Liver Transplantation – Interim Analysis Of A Prospective Observational Study

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Introduction

SGLT2 inhibitors, including dapagliflozin (DAPA), were approved for chronic kidney disease due to their slowing the decline in estimated glomerular filtration rate (eGFR) and reducing the incidence of end-stage renal disease. However, it remains unclear whether SGLT2 inhibitors also protect from CNI nephropathy, a common complication following liver transplantation (LT). Additionally, safety concerns of SGLT2 arise from increased rates of urogenital infections in non-transplanted patients.

Methods

This prospective observational single center study recruited LT recipients from 08/2021 to 10/2023, to whom DAPA was recommended because of CKD (eGFR 25 - 60ml/min/1.73) after LT.

Results

In total, DAPA was recommended to 206 patients with CKD after LT. Follow-ups (FU) at a median of 12 months were generated in 147 patients. 87 (59%) had stayed on DAPA until the FU, 24 (16%) had discontinued the treatment for various reasons. These two groups form the intention-to-treat-group (ITT, n=111). 36 (24%) patients had never begun the treatment (control group, CG). In total, 43 (39%) patients in the ITT and 10 (28%) patients in the CG experienced any kind of infection (p=0.234), but

this also included COVID-19 during the last phase of the pandemic (11% vs. 14%, p=0.616). In the ITT, 13 (12%; CG: n=1 (3%); p=0.582) patients experienced urinary tract infections and 5 (5%; CG: n=0; p=0.523) experienced genital mycosis (total urogenital infections: p=0.046). None of these urogenital infections led to hospitalization or death. The main reason for DAPA discontinuation were urogenital infections (n=5, 21%). Six patients died after DAPA recommendation (multiorgan dysfunction n=3, graft failure n=1, pneumonia n=1, unknown cause n=1).

The kidney function was stable with a slight non-significant decline in eGFR from DAPA recommendation to FU in patients with continued DAPA (n=87, -1ml/min/1.73; p=0,058).

Conclusion

DAPA use was not associated with severe infections or increased mortality after LT. Kidney function was stable within the short-term follow-up. Considering the study results from non-transplanted CKD patients, the earliest timepoint showing a renal benefit is expected after two years of DAPA treatment.

Y02-05

Comprehensive Bile Salt Analysis In Marginal Liver Allografts After Machine Perfusion – Translational Findings From A Multicentric, Randomized Controlled Trial (HOPE ECD-DBD)

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Introduction

Bile salt (BS) composition is crucial for hepatic and biliary viability, with bile salt toxicity implicated in various hepatic pathologies especially in liver transplantation with extended criteria donor (ECD) allografts from donors after brain death (DBD). Hypothermic oxygenated machine perfusion (HOPE) is an established preservation technique reducing ischemia-reperfusion injury and preventing biliary damage in ECD allografts. However, its influence on BS composition remains unclear.

Methods

Postoperative bile samples from 26 patients receiving ECD-DBD allografts within the HOPE ECD-DBD trial were obtained on postoperative day (POD) 1-7 and analyzed with mass spectrometry. 12 patients received a HOPE-treated allograft. Biliary BS composition were compared between HOPE and static cold storage (SCS) groups and associated with standard serum markers for hepatocyte and biliary injury. BS levels were also compared between organs with macrosteatosis ≥20%, and correlated with cold ischemia time (CIT), warm ischemia time (WIT), and donor age.

Results

BS levels significantly decreased over the first three days (POD-1 vs. POD-3,p<0.001; POD-2 vs. POD-3,p=0.049). The percentage of primary BS increased significantly from POD-1 to POD-3 (p=0.043), while secondary BS decreased (p=0.234). HOPE and SCS groups showed comparable BS compositions with significant declines from POD-1 to POD-3 (p=0.01 and p=0.035, respectively). Perfused organs showed an increase in the pro-

portion of primary (p=0.08) and decrease in secondary BS (p=0.09). Hydrophobic BS on POD-1 correlated significantly with ALP levels on POD-2 (p=0.017, r=0.464), POD-3 (p=0.008,r=0.506), and POD-7 (p=0.016, r=0.467) respectively. Biliary hydrophobic BS correlated with CIT duration on POD-1 (p=0.126) and POD-2 (p=0.008) but not with WIT or donor age. Allografts with macrosteatosis >20% had higher proportions of hydrophobic BS (p=0.009) and cholic/chenodeoxycholic acid ratio (p=0.039).

Conclusion

Hydrophobic and hydrophilic BS are significantly altered in HOPE-treated allografts. The present translational findings from the HOPE ECD-DBD trial highlight significant changes in BS composition and protective effects of HOPE in liver transplantation.

Y02-06

Comparison Of Immediate Release (IR) Tacrolimus Vs Extended Release (XR) LCP-Tacrolimus– A Single-Center Retrospective Observational Cohort Study

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Introduction

Tacrolimus remains an integral component of the standard immunosuppressive regimen after kidney transplantation. The aim of this study was to compare pharmacokinetic and clinical endpoints in kidney transplant recipients (KTR) receiving immediate release (IR) tacrolimus vs extended release (XR) LCP-tacrolimus for maintenance immunosuppression.

Methods

Patients ≥18 years, who received their first kidney transplant at Charité Universitätsmedizin Berlin between 01.01.2015 and 01.01.2022 and were continuously prescribed either IR tacrolimus or XR tacrolimus throughout the first 365 days posttransplant were eligible for study inclusion. Non-kidney transplant recipients, patients with allograft loss or death within one year after transplantation were excluded. For analysis of pharmacokinetic parameters ≥3 ambulatory tacrolimus measurements between month 6 and month 12 posttransplant were required. Clinical endpoints were assessed by Kaplan-Meier analysis and log-rank test.

Results

Overall, 529 KTR were included in the final analysis (317 IR tacrolimus, 212 XR tacrolimus). XR tacrolimus displayed higher concentration/dose ratio (fast metabolizer status, ratio < 1.05 ng/mL×1/mg: 17% for XR tacrolimus vs 22% for IR tacrolimus) and higher coefficient of variation (mean 0.28 for XR tacrolimus vs 0.21 for IR tacrolimus, p<0.05). In the Kaplan-Meier analysis over 3 years follow-up, patients on XR tacrolimus showed less biopsy-proven rejections (p=0.038), whereas there was no significant difference regarding survival (p=0.25) or death-censored graft loss (p=0.28).

Conclusion

In this single-center retrospective observational cohort study, patients receiving XR tacrolimus displayed a higher concentration/dose ratio and less biopsy-proven rejections in the early phase posttransplant.

Y02-07

Treating Refractory BK Virus Nephropathy With Allogenic BK Virus-Specific T Cells In Kidney Transplant Recipients

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Introduction
In kidney transplant recipients, refractory BK virus nephropathy (BKVNP) poses a serious risk for graft loss. Since there are no targeted therapies available, we investigated the effects of allogeneic BKV-specific T cell transfer on graft function, the amount of BKV-specific T-cells and BKV replication in patients' blood.

Methods
We included three kidney transplant recipients with refractory BKVNP, which was defined by persistent BKV replication above 1000 IU/ml despite minimal possible immunosuppression, absence or low levels of BKV-specific T-cells and histologically confirmed BKVNP. For two of the three patients, virus-specific T-cell-donors were selected from the third party T-cell donor registry (allo-CELL), after ensuring the best possible HLA compatibility with the recipient and the transplanted organ. For one patient, the related living organ donor was selected as the T-cell donor, thus ensuring a haploidentical T-cell transfer. BKV-specific T-cells were produced by leukapharesis and consecutive short-term stimulation with LT and VP1 overlapping peptide pools following cytokine selection and magnetic separation on a CliniMACS Prodigy device. The patients received at least four T-cell transfusions every three weeks. The BKV load was sequentially quantified by qPCR and the level of BKV-specific T-cells was enumerated using interferon-γ Elispot assay.

Results
We observed a significant decline in the BKV load in all the three cases (decrease by 93.16%, 78.10%, 71.11% when compared to the viral load before initiation of therapy), together with a significant increase in the BKV-specific T-cells in the recipients' blood. The declining BKV load was most pronounced in the haploidentical transplant patient (by 93.16%), thus highlighting the relevance of HLA-compatibility to ensure an adequate T-cell milieu. The graft function remained stable throughout the course of therapy. No infusion-related adverse events were observed.

Conclusion
BKV-specific T-cell therapy is a promising new approach to treat patients with refractory BKVNP. The selection of suitable patients may be conducted based on the quantification of BKV-specific T-cells, BKV blood levels as well as allograft function and histology.

Y02-08

Restricting Datasets To Classifiable Samples Augments Discovery Of Biomarkers

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Introduction

Diseases are typically heterogeneous and complex in clinical presentation, severity and response to therapy. Biomarkers often reflect this variability, especially compared to their regulated behaviour in healthy individuals. This leads to a common difficulty that frustrates biomarker discovery and interpretation: Unequal dispersion of immune disease biomarker expression between patient classes necessarily limits a biomarker's informative range. Thus, diagnostic biomarkers are often overlooked if they are informative in only a subset of patients. By capturing information about the precise nature of a biological system through measuring biomarkers, we can develop diagnostic or prognostic models to guide personalized treatment decisions.

Methods

We recently introduce dataset restriction, a procedure that splits datasets into classifiable and unclassifiable samples [1]. Restriction allows us to identify biomarkers even if they are informative in only a subset of patients. For this, we identify and restrict samples to the biomarker range that optimally separates the patient classes. With this, restriction reliably identifies classical and otherwise disregarded biomarkers, returns interpretable "informative ranges" where a biomarker is predictive of a class and improves multivariate models.

Results

We applied dataset restriction to synthetic and real data and found its utility in transcriptomic, proteomic, microbiomic, flow and mass cytometric public and own datasets. The method is applicable as a self-contained biomarker discovery tool or as a pre-processing step for building multivariate models. We published an R package to apply dataset restriction and provided a detailed tutorial on its application.

Conclusion

Dataset restriction augments the discovery of immune disease biomarkers, increases predictive certainty for classifiable samples and improves multivariate models incorporating biomarkers with a limited informative range. This principle can be directly applied to any classification task.

Reference

[1] Glehr, G, Riquelme, P, Kronenberg, K, Lohmayer, R, López-Madrona, V J, Kapinsky, M, Schlitt, H J, Geissler, E K, Spang, R, Haferkamp, S, & Hutchinson, J A (In Press), Restricting datasets to classifiable samples augments discovery of biomarkers, Nature Communications

Y02-09

Nicotinamide Adenine Dinucleotide Could Be A Marker For Assessing Organ Viability And Ischemia Reperfusion Injury During Normothermic Machine Perfusion – An Ex Vivo Small Animal Study

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Introduction

Due to organ shortage, the use of extended criteria (ECD) grafts is becoming more common in liver transplantation. Machine perfusion (MP) can be used for quality assessment, which is vital as ECD grafts are more susceptible to ischemia-reperfusion injury (IRI)[1] . Intracellular nicotinamide adenine dinucleotide (iNAD$^+$) has been a focus of recent research as changes in NAD have

been linked to ageing and IRI response [2]. We aimed to investigate iNAD⁺ as a potential biomarker for assessing graft function and transplant performance using an established small animal model of normothermic MP[3], emulating ECD criteria such as donor age, prolonged static cold storage (pSCS) and donation after circulatory death (DCD).

Methods

Liver grafts from 72 Sprague Dawley rats (3- and 12-month-old) undergoing 6 hours of normothermic MPs were analyzed. DCD groups were DCD (n=24) and pSCS (6h vs. 12h, n=24), Donation after Brain Death (DBD) (n=24) served as a control. iNAD⁺ was measured according to an established protocol[4, 5]. Groups were compared using the Kruskal-Wallis and Tukey's test.

Results

Perfusate and tissue analyses indicated pronounced damage in ECD grafts compared to the DBD controls. iNAD+ levels were significantly lower in liver tissue of elderly DCD donors compared to the young controls (DCD 65µM, IQR 34µM vs. DBD = 102µM, IQR 37µM, p = < 0.001), with similar trends in perfusate samples (DCD = 0.25µM, IQR 0.06µM vs. DBD = 0.58µM, IQR 0.56µM, p = 0.056). Furthermore, we found a trend towards lower tissue iNAD+ levels (6h SCS =116µM, IQR 29µM vs. 12h SCS =84µM, IQR 32µM, p = 0.057 in grafts with pSCS).

Conclusion

Tissue and perfusate iNAD+ levels correlated well with the level of induced damage prior to liver reperfusion in our small animal MP model. iNAD+ levels in perfusate could provide an additional method to assess organ performance during MP. Further research should explore the specificity of iNAD+ for predicting short term graft function in addition to supplementation as a potential means to dampen the impact of IRI.

References

[1] Okaya, T., et al., *Age-dependent responses to hepatic ischemia/reperfusion injury.* Shock, 2005. **24**(5): p. 421-427.

[2] Massudi, H., et al., *NAD+ metabolism and oxidative stress: the golden nucleotide on a crown of thorns.* Redox Rep, 2012. **17**(1): p. 28-46.

[3] Nösser, M., et al., *Development of a Rat Liver Machine Perfusion System for Normothermic and Subnormothermic Conditions.*Tissue engineering. Part A, 2020. **26**(1-2): p. 57-65.

[4] Brunnbauer, P., et al., *The nanomolar sensing of nicotinamide adenine dinucleotide in human plasma using a cycling assay in albumin modified simulated body fluids.* Sci Rep, 2018. **8**(1): p. 16110.

[5] Saqr, A.A., et al., *Optimized protocol for quantification of extracellular nicotinamide adenine dinucleotide: evaluating clinical parameters and pre-analytical factors for translational research.* Front Med (Lausanne), 2023. **10**: p. 1278641.

Y02-10

Histological Analysis Of Porcine Hearts Preserved Via *Ex-Vivo* Normothermic Heart Perfusion With Perfluorocarbon-Based Artificial Oxygen Carriers

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Introduction

Normothermic machine perfusion (NT-MP) has emerged as new technology for organ preservation in clinical practice. Instead of reducing the metabolic activity by lowering the temperature as in static cold storage, the philosophy of NT-MP is to meet the metabolic demand of an organ.[1] Since NT-MP is limited to erythrocate-enriched perfusion solutions, perfluorodecalin-based albumin-derived artificial oxygen carriers (A-AOC) are a potential supplement for perfusion solutions to counteract the organ donor's blood deficiency.[2] Our group

previously demonstrated the successful preservation of isolated rat hearts.[3] The aim of this project was to investigate the integrity of substitutes.

Methods

An experimental set-up was established for normothermic machine perfusion of porcine hearts with a perfusion medium enriched with A-AOCs. Hemodynamic and biochemical investigations of the preservation fluids were studied by blood gas analyzer and photometry (respons 920). Additionally, biopsies were taken after perfusion to determine wet-dry-ratios and for histological analysis.

Results

In a pilot study, the contractility of porcine heart was maintained for at least three hours by NT-MP with a preservation solution. The integrity of the tissue was assessed by wet-dry-ratios and cardiac morphology was examined by HE staining.

Conclusion

We will explore the potential of A-AOCs to reduce reperfusion-associated acute myocardial infarction (repAMI) during *ex vivo* heart perfusion based on histological analysis and edema formation. Our group has previously shown that isolated porcine kidneys exhibit intact renal morphology after perfusion with A-AOCs.[4] Therefore, NT-MP with A-AOCs is expected to preserve cardiac morphology.

References

1. N. Pizanis, A. Dimitriou, A. Koch, P. Luedike, M. Papathanasiou, T. Rassaf, A. Ruhparwar, B. Schmack, A. Weymann, K. Ferenz, M. Kamler in *IJC Heart & Vasculature***2023**, 47, 101233.
2. K. Ferenz, O. Karaman, S. B. Shah in *Nanotechnology for Hematology, Blood Transfusion, and Artificial Blood*, Elsevier, **2022**, pp. 397–427.
3. A. Wrobeln, K. D. Schlüter, J. Linders, M. Zähres, C. Mayer, M. Kirsch, K. B. Ferenz in *Artificial cells, nanomedicine, and biotechnology***2017**, 45, 723.
4. T. Rother, C. Horgby, K. Schmalkuche, J. Burgmann, F. Nocke, J. Jägers, J. Schmitz, J. Bräsen, M. Cantore, F. Zal, K. Ferenz, R. Blasczyk, C. Figueiredo, *Frontiers in Transplantation***2023**, 2:1183908.

Poster Presentation

Poster Session 01: Liver

PV01-01

Three Decades Of Liver Transplantation For Biliary Atresia: Outcomes Of 3721 Liver Transplants From CTS Registry

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Introduction
Biliary atresia (BA) is one of the most common indications for pediatric liver transplantation (LT). This registry study presents the challenges and achievements in the field of LT for BA within the last 30 years.

Methods
Data obtained from the Collaborative Transplant Study (CTS) on all patients undergoing LT for BA performed from 1 January 1990 to 31 December 2019 in 69 centers from 22 countries were analyzed. Graft survival was defined as a combined endpoint, defined as the time from LT to either patient's death or re-transplantation or last known contact (whichever came first).

Results
Three thousand seven hundred and twenty-oneLTs (1667 male, 2054 female) for biliary atresia were documented within three decades. Less than half of the recipients (1589, 42.7%) were under 12 months of age at the time of transplantation for biliary atresia, followed by children of age group 1-2 years old (1129, 30.3%). Most grafts came from deceased donors (2829, 76%); pediatric / adolescent donors comprised almost half (1290, 46%) of the deceased donor population. The most common graft types used in LT for biliary atresia were the split grafts from deceased donors (1646, 58%), followed by whole organs (1031, 36%), and grafts from living donors (892, 24%; female to male ratio 1.3). Reduced size (as well as otherwise anatomically modified) deceased donor grafts were used in only around 5% of LTs (n=150). 3298 (88.6%) were primary LTs; 423 (11.4%) were re-LTs. Re-LTs showed a down-trend to almost a half from 14.3% in 1990-1999 compared to 7.7% within 2010-2019. Being transplanted in 1990-1999, donor age older than 40 years (50 years in living donor LT), cold ischemia times longer than 10 hours (only in deceased donor LTs), ABO-incompatibility, high urgent LTs (only in deceased donor LTs), and Re-LTs were independent risk factors for graft loss.

Conclusion

Excellent outcomes have been achieved through LT for BA patients over the last three decades with significantly improved 5-year survival within the last decade, where the survival difference between the deceased and the living donor LTs narrows, so that it loses the statistical significance.

PV01-03

Enhanced Recovery Protocol After Liver Transplantation – A Prospective Analysis

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Introduction
Enhanced Recovery After Surgery (ERAS) is a multimodal approach for almost all types of surgical procedures, including liver transplantation (LTx). Here we report on a prospective analysis of an ERAS protocol in liver transplantation in order to identify challenges in this field.

Methods
An ERAS protocol based on SOPs in liver transplantation, including donor, preoperative, anesthetic, intraoperative, and postoperative data, was developed and implemented in our center from 2018 to 2023. Information regarding the enrolled patients' was collected. The operative and post-operative characteristics and length of hospitalisation was documented. All patients were followed-up for 180 days after discharge.

Results
TheERAS protocol was applied prospectively in 68 LTx patients. Mean patient age was 49.58 years, (80.89%) were male. Mean BMI was 24.14 kg/m^2. Mean MELD score was 15.41, 3 patients had a MELD score higher than 30. 53 had HBV cirrhosis, 24 had hepatocellular carcinoma. 5 patients were diagnosed with alcohol related cirrhosis respectively primary biliary cirrhosis, autoimmune disease and drug induced cirrhosis was 1, respectively. Mean age of the donors was 47 years, 85% were male, 60% DBD, 39% DCD and 1% DBCD. Cause of death was cerebral hemorrhage 55%, craniocerebral trauma 31%, 14% had cerebral infarction, CO intoxication, organophosphorus poisoning or hypoxic ischemia. The mean operation time was 6.73 hours, average anhepatic time was 67.51 minutes. No patient suffered from intraoperative hypothermia. Tracheal extubation was performed in the ICU within 6 hours post operation and the average ICU/IMC stay was 4.59 days. None of the patients required re-intubation. Immunosuppression was basiliximab, tacrolimus (C0 3-8 ng/ml), mycophenolate mofetil and steroids. No acute rejection was reported and patient and graft survival was 98.5% at 180 days.

Conclusion
We prospectively analyzed a SOP based ERAS protocol in LTx, containing preoperative, anesthetic, intraoperative, and postoperative procedures. Our study revealed that the proposed ERAS approach in LTx is feasible, reducing the utilization of medical resources promoting better recovery and short term outcomes under local conditions.

PV01-04

Sex-Specific Differences In Gene Expression In Livers Of Male And Female Fisher Rats

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Introduction
Sex dependent differences of gene expression in the liver are not sufficient studied, especially after liver transplantation. Differences at the molecular genetic level may have a significant influence on the outcome after transplantation. The aim was to assess sex specific differences in gene expression in Fisher rat liver tissues at a molecular level.

Methods
Male (n=5) and female (n=5) Fisher rats at the age of five months were euthanized and liver tissue was obtained. RNA was isolated and quality controlled. RNA-Seq was executed by NGS. Library creation was done utilizing Lexogen 3' FWD method, sequencing was conducted by Illumina Sequencing. Data mapping and statistical analysis was done with Enhanced Volcano on R. Kegg and GO analysis was conducted for gene enrichment.

Results
We conducted a comprehensive analysis of the ten most significantly ($p < 10^{-100}$, lowest p-value: $p < 10^{-250}$ with a $\log_2$FC) expressed genes between female and male rat livers. Prominently expressed genes in female liver tissue are, among others involved in the eicosanoid and prostaglandin pathways. Marked expression of sex-specific sulfotransferases and CYP450 enzymes was notable. Other highly expressed genes in female liver tissue areassociated with chemokine activity, macrophage differentiation, activation of PMNCs, NK cells, estrogen and blood coagulation. Elevated expressed genes in male liver tissue are, among others, involved in peroxidase, oxidoreductase and redox signaling pathways related genes.

Conclusion
This study suggests that sex dependent differences in gene expression play an important role for pathways, which might have a relevant influence on the outcome after liver transplantation. Sex specific gene expression analyses at different times after sex-mismatched and sex-matched liver transplantations might give significant information, which can help to improve the outcome.

PV01-05

Warm Ischemia Time Correlates With Intraoperative Blood Transfusion

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Introduction
The recipient warm ischemia time (WIT) is a highly relevant factor with utmost clinical importance in liver transplantation (LT). Another factor that may influence the postoperative outcome is the amount of intraoperative blood transfusion. The relationship between WIT and intraoperative transfusion has only been researched to a limited extent.

Methods
A retrospective analysis was conducted on data pertaining to180 recipients of LT between 2013 and 2022 at the University Hospital of Bonn. The analysis focused on the correlation between WIT and intraoperative blood transfusion. The patient cohort was divided into quartiles: Q1: WIT ≤33min, Q2: WIT 34-38min, Q3: WIT 39-46min and Q4: WIT >46min. Additionally, the occurrence of major postoperative complications (at least Clavien/Dindo grade IIIb) and vascular occlusions was also evaluated.

Results
Intraoperative transfusions were used with increasing frequency with longer WIT time. Median RBC and FFP transfusion per group were respectively: 7 and 8 units (Q1), 6 and 7 units (Q2), 7 and 8 units (Q3) and 11 and 16 units (Q4) (p=0.030 and p=0.002). The median of platelet transfusions was 2, 1.5, 2 and 2.01 units in Q1,Q2, Q3 and Q4 (p=0.063). Splitting the cohort on the median into Q1/2 and Q3/4, RBCs, FFPs and platelet transfusions have a higher frequency at Q3/4 (p=0.036; p=0.010; p=0.010). Major complications occurred in 47% of the recipients in Q1/2, compared with 63% in Q3/4 (p= 0.028). Vascular occlusions were found in 7% in Q1/2 and 10% in Q3/4 (p=0.5).

Conclusion
A significant correlation has been identified between prolonged WIT and the administration of intraoperative RBC, FFP, and platelet transfusions. This is evident in both the division of the patient cohort into quartiles based on the duration of WIT and in splitting the cohort along the median. Additionally, major complications and vascular occlusions were observed to be more prevalent in patients with prolonged WIT. Further studies with larger numbers of patients are necessary to evaluate the relationship between WIT and intraoperative transfusions with greater precision.

PV01-06

HDTACRO: A Prospective Study On The Impact Of Tacrolimus-Based Immunosuppression After Liver Transplantation

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Introduction
The HDTACRO study evaluates the impact of Tacrolimus-based immunosuppression in the Heidelberg liver transplant cohort. The study focuses on improving long-term outcomes post-orthotopic liver transplantation (OLT) by balancing the efficacy and toxicity of Tacrolimus, a critical immunosuppressant with significant inter- and intra-individual variability.

Methods
This monocentric, prospective, non-interventional study included 100 OLT patients treated with oral Tacrolimus-based immunosuppressants (Prograf or Envarsus). Key data collected included demographic information, underlying liver disease, and preoperative evaluations. The primary endpoint was the number of dose adjustments required to achieve target trough levels of Tacrolimus. Patient recruitment spanned a specific period (details on exact recruitment period were not provided), and follow-up lasted for six months post-transplantation.

Results
The study included 56 patients who received once-daily Envarsus® and 44 who received twice-daily Prograf®. Both groups had a median of five dose adjustments over six months. There were no significant differences in therapy adherence or medication timing between the groups. Six patients (four from the Envarsus group and two from the Prograf group) were converted to cyclosporine due to various complications. In the Envarsus group there was one case of re-transplantation and cases of sepsis-associated mortality. Laboratory findings indicated that the Envarsus group had lower ALT, AST, and creatinine levels over time compared to the Prograf group, with significant differences observed in GFR and the ratio of Tacrolimus concentration to dosage.

Conclusion
The study indicates that while both Tacrolimus formulations require multiple dose adjustments, Envarsus may offer better kidney function and liver enzyme profiles. This suggests potential benefits in selecting specific Tacrolimus formulations based on individual patient profiles and therapeutic needs.

PV01-07

Update: High-Volume Single Center Analysis Of Hypothermic End-Ischemic Liver Preservation: Dual HOPE Beats It All

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Introduction
Machine perfusion techniques are increasingly used in donor organ preservation and end-ischemic hypothermic oxygenated machine perfusion (HOPE) becomes standard of care in an increasing number of transplant centers. In this study, we conduct a comparative analysis of mono HOPE (mHOPE) and dual HOPE (dHOPE). Our study is based on our experience from late 2019 to present at the LMU Munich.

Methods
In this retrospective analysis, we evaluate the impact of mHOPE and dHOPE on liver transplant outcomes. Our study population includes 161 patients who received liver grafts preserved with end-ischemic HOPE (87 mHOPE and 74 dHOPE) from late 2019 to present. We analyze multiple parameters including ICU length of stay, hospital length of stay, and biliary complications.

Results
Our results from liver grafts preserved with end-ischemic HOPE show that dHOPE is the superior modality compared to mHOPE. Although there was no significant difference in ICU length of stay, data show that hospital length of stay and biliary complications were in favor of dHOPE.

Conclusion
To our knowledge, this is the largest comparative analysis highlighting the superiority of the modality dHOPE over mHOPE in end-ischemic hypothermic graft preservation before liver transplantation. The reduction of hospital length of stay and biliary complications argues for conducting dHOPE as the standard procedure for end-ischemic hypothermic organ preservation before liver transplantation.

PV01-08

A 10-Year Single Centre Analysis Of Liver Retransplantation – Indications And Outcomes

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Introduction
Re-transplantation is the only form of treatment for patients with irreversible graft failure after liver transplantation (LT). Primary nonfunction or vascular thrombosis are the leading indications for liver re-transplantation (ReLT). Due to and despite long-term success of LT, an increasing number of patients with end-stage liver graft disease years after LT present in clinical practice. However, indication criteria for ReLT in this group of patients are variable and part of ongoing interdisciplinary discussions.

Methods
Retrospective data analysis identified 693 LTs at Hannover Medical School from January 1st, 2008, to December 31st, 2017. Patients undergoing ReLT were divided into two cohorts, depending on the duration from primary LT to ReLT. Cohort 1 included patients receiving ReLT within one year after primary LT. Patients with ReLT following more than one year after primary LT were included in cohort 2. The analysis of both groups included patient, donor, and graft-specific characteristics.

Results
Of the 693 patients undergoing LT, 8 % (n=56) needed retransplantation within one year after LT (cohort 1) and 2.3 % (n=16) longer than one year after LT (cohort 2). The average time to ReLT was 364.65 days. Leading causes for ReLT in cohort 1 were primary nonfunction (n=29), vascular complications (n=16), and extensive graft necrosis (n=11). Leading cause for ReLT in cohort 2 were cirrhosis of the graft and recurrence of the primary disease. The mean survival following ReLT in all patients was 364.92 days after ReLT with a 5-year mortality rate of 51.39% (n=37). Mortality in cohort 1 and 2 was 60% and 18.7%, respectively. The leading causes of death were sepsis (cohort 1: 13 patients; cohort 2: 2 patients) and cardiovascular complications (cohort 1: 6 patients; cohort 2: 1 patient).

Conclusion
Liver retransplantation, even long-term after initial LT, represents a suitable treatment option for selected patients. However, this approach is associated with increased morbidity and reduced postoperative survival. In light of organ shortage and increased morbidity of candidates listed for ReLT, there is an urgent need to identify optimal selection criteria.

PV01-09

Preoperative Transarterial Chemoembolization Results In Improved Disease-Free Survival After Liver Transplantationfor Hepatocellular Carcinoma

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Introduction

Liver transplantation (LT) is the treatment of choice for the patients suffering from hepatocellular carcinoma (HCC), who are not eligible for liver resection. Transarterial chemoembolization (TACE) can be used as a bridging therapy for patients fulfilling the Milan Criteria (MC) or for downstaging for those exceeding MC. In this setting, TACE aims to prevent tumor progress and thus waitlist dropout. However, the effect of preoperative TACE on post-operative recurrence has not been fully investigated. Here, we present the effect of TACE on HCC recurrence following LT in patients both fulfilling and exceeding MC.

Methods

The study was designed as a retrospective single center analysis. Patients with confirmed HCC undergoing LT between January 2008 and December 2021 were included in the analysis. The number and size of the tumors, as well as fulfilling MC were assessed by a senior radiologist using the latest cross-sectional imaging prior to the LT.

Results

During the study period, 80 HCC patients with a median age of 60 years (29-73) were transplanted (18 f / 62 m). The most common underlying disease was alcoholic liver disease (30%) followed by Hepatitis B and C (27.5% and 16.3%, respectively). A total of 30 patients fulfilled MC, whereas 40 patients exceeded MC. By 10 Patients, MC could not be assessed due to the missing data. The median number and size of the tumor were 2 (1-19) and 35.5 mm (14.8-148 mm), respectively. Thirty-nine patients received TACE prior to the transplant, of which 16 were inside MC and 19 outside MC. The 5-year survival of the entire cohort was 66.5%, whereas patients with and without TACE had 5-year survival of 76% and 55.8% respectively (p=0.076). However, patients with TACE showed significant better 5-year disease-free survival (73.6%) compared to the patients without TACE (46%, p<0.05), especially for those exceeding MC (88.9% vs. 33.3%, p<0.001).

Conclusion

Although preoperative TACE showed no effect on long-term survival after LT for HCC, it resulted in better 5-year disease free survival irrespective of MC. Thus, TACE should be considered more stringent as bridging or downstaging strategy in waitlist patients.

PV01-10

Retransplantation Despite Candida Bacteremia – When Tips Is The Bad Guy

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Introduction

The transjugular intrahepatic portosystemic shunt (TIPS) is frequently used to decompress portal hypertension. The entity of persistent TIPS infection is a rare but serious complication after TIPS insertion in native liver. Today, these are mainly bacterial infections caused

by gram-positive cocci. Candida infections were more common in the past, but are now a rarity. The use of a TIPS in a transplanted liver has been the subject of controversy for years. Earlier data show that this intervention achieves good results in refractory ascites or in the presence of portal vein thrombosis, but the risk of infection is increased because of necessary immune suppression.

Methods
We present the case of a patient who received a liver transplant in 2020 due to cirrhosis due to hepatitis C. In 2022, the patient suffered a portal vein thrombosis during the transplant, so a TIPS system was inserted as part of an individual cure attempt. Approximately four weeks later, the patient developed recurrent fever and increasing fatigue. Blood cultures were positive for Candida albicans. Fungal infection of TIPS could not be detected in several samples. However, reactivation occurred again after discontinuation of antifungal treatment. After excluding other causes of bacteremia, a retransplant was performed in March 2023. Histological examination of the explant revealed extensive fungal infection of the TIPS and surrounding tissue.

Results
With good transplant function, no reactivation of Candida albicans infection has occurred so far.

Conclusion
The risk of TIPS infections is increased in immunosuppression. Liver transplant patients are susceptible to atypical infections such as Candida albicans bacteremia. The decision for a repeat transplant must be made on an interdisciplinary basis and requires a high level of expertise. It should always be considered as an exceptional treatment.

PV01-12

End-Ischemic Pharmacological Cocktail Treatment To Mitigate Rewarming/ Reperfusion Injury

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Introduction
Increasing shortage of donor organs leads to the acceptance of less than optimal grafts for transplantation, up to and including organs donated after circulatory standstill of the donor. Therefore, protective strategies and pharmacological interventions destined to reduce ischemia induced tissue injury are considered a worthwhile focus of research. The present study evaluates the potential of a multidrug pharmacological approach as single flush at the end of static preservation to protect the liver from reperfusion injury.

Methods
Livers were retrieved from male Wistar rats 20 min after cardiac standstill. The organs were cold stored for 18 h, flushed with 20 ml of saline, kept at room temperature for 20 min, and reperfused at 37°C with oxygenated Williams E solution. In half of the cases, the flush solution was supplemented with a cocktail containing metformin, bucladesine and cyclosporin A.

Results
Upon reperfusion, treated livers disclosed a massive mitigation of hepatic release of alanine aminotransferase and aspartate aminotransferase, along with a significant approximately 50% reduction of radical mediated lipid peroxidation, caspase activation and release of TNF-alpha.

Conclusion
Even after preceding cold preservation, a pharmacological cocktail given as single flush is capable to mitigate manifestations of reperfusion injury in the present model.

PV01-13

Osteopenia Is Associated With Impaired Outcome After Deceased-Donor Liver Transplantation

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Introduction
Alterations in body composition have been linked to both perioperative and long-term outcomes subsequent to orthotopic liver transplantation (OLT). Nevertheless, the potential predictive role of recipient bone mineral density (BMD) in clinical outcomes following OLT remains uncertain. In this study we aimed to explore the role of BMD as a prognostic factor in patients undergoing OLT after brain death donation, assessed using preoperative computed tomography (CT), in the context of major perioperative morbidity (Clavien Dindo >3b and Comprehensive Complication Index (CCI)), mortality, and long-term graft and patient survival.

Methods
A total of 480 patients who underwent OLT during the period from 2010 to 2023 at the University Hospital RWTH Aachen were included into the retrospective analysis. Preoperative computed tomography-based segmentation was used to measure BMD at the level of the 12th thoracic vertebra. Osteopenia was defined based on gender-based pre-described cutoffs.

Results
In our cohort, osteopenia was highly prevalent (48%) and osteopenic patients experienced significantly greater major postoperative morbidity (Clavien–Dindo $\geq$ 3b; 57% vs. 47%, p=0.026). Correspondingly, in-hospital CCI differed significantly (45 [30-88] vs. 49 [24-75], p=0.019), and patients suffering from osteopenia required more perioperative red blood cell (8[4-13] vs. 6[3-10] units, p=0.013) and fresh frozen plasma (18[14-75] vs.16 [12-22] units, p=0.026) transfusions.

Furthermore, patients with osteopenia exhibited significantly inferior overall survival (91$\pm$4.2 vs. 112$\pm$3.9 months, p=0.001) and impaired graft survival (91$\pm$4.1 vs. 105$\pm$4.1 months, p=0.037). In our multivariable model, osteopenia was confirmed as an independent risk-factor for inferior overall survival (Hazard-ratio 1.586, p = 0.006).

Conclusion
The presence of osteopenia could serve as a valuable and easily assessable predictor for both perioperative and long-term outcomes in patients undergoing OLT, thus underlining the predictive significance of body composition in this context. Further research is warranted to validate these findings.

PV01-14

Impact Of Incorrect Volumetry On Recipient Outcome After Living Donor Liver Transplantation – Higher Accuracy By Using Volumetry-Assist Software

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Introduction
Liver transplantation (LT) is an established treatment for patients with end-stage liver disease. Due to the shortage of suitable organs living donor liver transplantation (LDLT) has emerged as an equivalent alternative. Assessing the size of the future liver remnant and graft through preoperative volumetry is essential for the outcome after LDLT. While the current gold standard for this is manual CT-volumetry (MV), the use of volumetry-assist software (VS) may replace the previous routine. In this study, we analyzed whether VS is superior to MV in terms of accuracy and thus may improve postoperative outcomes after LDLT.

Methods
We conducted a retrospective analysis of 133 LDLTs, which were performed at University Hospital Regensburg in the years 2004 to 2021. Recipients were assigned to a correct, underestimated, or overestimated mea-

surement group based on MV. Postoperative outcomes were compared between these groups. Additionally, volumetric assessment by VS using Syngo.via Liver Analysis (Siemens Healthineers) was performed blinded.

Results

Underestimated MV was significantly more common in left-lateral donations, but the overall outcome remained comparable to the correct MV group. However, significantly higher rates of abdominal compartments and delayed wound closures were seen for a GRWR > 4, which occurred in 33 cases (70.2%) of underestimated MV. In 66.6% (n=22) of these cases a correct result would have been achieved using VS. In contrast, overestimated MV was significantly more frequent in adults and right-sided hemihepatectomies. Postoperatively, a significant increase in thrombosis of the hepatic artery, bile leakage, dialysis requirement and listing for re-LTx in HU status was observed. Overall, MV was correct in 35.3% of cases (n = 47), while VS measurement achieved an accurate result in 66.9% of cases (n = 89).

Conclusion

Our study confirmed a higher accuracy for liver graft measurement using VS compared to currently common MV. This approach may reduce the incidence of postoperative complications, particularly due to underestimated volumes in children resulting in a GRWR > 4 and overestimated volumes in adults.

PV01-15

Identification Of Risk Factors For The Appearance Of Diaphragmatic Hernia After Pediatric Liver Transplantation

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Introduction

Diaphragmatic hernia is a rare and potentially life-threatening complication after pediatric liver transplantation, but there is a lack of data about risk factors. The objective of this study was to analyze risk factors and clinical course of patients with and without development of diaphragmatic hernia.

Methods

In this retrospective study we included all pediatric (<18 years) patients from our center receiving a liver transplantation from January 2008 until May 2024. Putative risk factors and data of the clinical course were collected from digital and handwritten patient records for all cases. Resulting data were presented comparing the two groups with and without diaphragmatic hernia.

Results

Within our study period, we identified 259 pediatric liver transplantations. In 14 cases, the patient developed a diaphragmatic hernia during the study period. According to our ongoing collection of data there is no resilient comparison of the two groups yet but we can characterize a typical patient with diaphragmatic hernia:

- female (79 %),
- no visible diaphragmatic damage during transplantation (100 %),
- appearance of diaphragmatic hernia during the first year after transplantation (79 %),
- nausea and vomiting are the leading symptoms (50 %),
- hernia is located on the right side of the diaphragm (64 %),
- incarceration may occur (36 %),
- therapy of the hernia without a mesh (64 %).

Conclusion

As diaphragmatic hernia is a rare but dangerous complication after pediatric liver transplantation it is most important to keep this complication in mind - especially when children present with nausea or vomiting and if patients fulfill risk factors identified in this study.

PV01-16

Outcome Of Combined Pediatric Liver Transplantation And Hematopoietic Stem Cell Transplantation: A Single-Center Case Series

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Introduction
Solid organ transplantation (SOT) in children with hematopoietic stem cell transplantation (HSCT) is rarely performed, with an estimated prevalence of < 0.1 %. Liver transplantation (LT) is the most common SOT in children with HSCT, which poses unique challenges, including immunosuppression (IS), graft selection, and timing.

Methods
Retrospective cohort analysis of children receiving a LT and HSCT at a large academic transplant center from 2017 to 2023.

Results
Among 16 children who received a LT, two (12.5%) underwent both LT and HSCT.

Patient 1**:** LT 3 years post-allogeneic HSCT (HLA-identical brother) due to severe combined immunodeficiency of unknown etiology at the age of 6 years, and progressive cholestatic liver disease secondary to chronic *Cryptosporidia* positive cholangitis and potential additional drug induced liver injury. Left lateral split liver transplantation (LLS-LT) from a deceased donor (DD). Post-LT, the child experienced biliary complications requiring percutaneous biliary drainage for 12 months. 4 years post-LT graft function is excellent with no chronic or acute changes on biopsy.

Patient 2: Acute liver failure and aplastic anemia at the age of 3.5 years with listing for high-urgent LT and simultaneous preparation for HSCT. She first received a LLS-LT from a DD, followed by an allogeneic HSCT from her HLA-identical brother four weeks later. Her post-LT and HSCT follow-up, was uneventful, with good engraftment and graft function, and no chronic or acute changes on biopsy 3 years post-LT.

IS consisted of Basiliximab, short term corticosteroids (3 months), and Tacrolimus for both children. Conditioning regimens included Fludarabine and Treosulfan, with the addition of ATG in patient 2. Multidisciplinary work up and care was necessary in both cases.

Conclusion
We report two patients who underwent LT and HSCT at our center over the past 7 years. The medium-term follow-up was mainly uneventful, and both patients present with excellent graft function. These cases demonstrate the value of LT in children with primary immunologic or hematologic diseases and underscore the importance of a multidisciplinary approach with all necessary services available on site.

PV01-17

Assessment Of The Impact Of Donor Age And Prolonged Warm Ischemia On Liver Graft Viability -Ex Vivo Liver Machine Perfusion Studies In Sprague Dawley Rats

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Introduction

In liver transplantation, there is a critical mismatch between organ supply and demand, worsened by the aging population in the Western World. [1] Increased use of grafts from older donors [2] raises risks of complications from ischemia-reperfusion injury. [2] Normothermic ex vivo liver machine perfusion (NMP) is a promising strategy to mitigate preservation injury by maintaining grafts under near-physiologic conditions. [4] Our aim was to investigate the effects of a combined damage model involving high donor age and prolonged warm ischemia time on graft viability and quality during NMP.

Methods

Twenty-four Sprague Dawley rats were divided by donor age (3 vs. 12 months) and NMP duration (3 vs. 6 hours). After circulatory arrest and 30 minutes of warm ischemia, grafts were perfused using a previously established dual vessel NMP system [5] supplemented with verapamil to prevent vasospasm. Bile, perfusate, dialysate and tissue samples were analyzed.

Results

Livers from elderly donors were heavier than younger ones (23.46g vs. 18.21g; $p < 0.001$). Perfusion pressures rose in both groups over time. Elderly livers required blood flow reduction at later time points and maintained target flow more consistently (83% vs. 33%). Livers in both groups cleared lactate, while elderly grafts presented with initially higher levels but converging by the end. ALT and AST rose during perfusion, with younger livers showing significantly higher AST levels (4328 vs. 3432 U/l; $p=0.041$). Grafts from elderly donors produced more bile, with highest production after 2 hours (84 vs. 39 mg/h; $p=0.044$). Overall, histology showed greater congestion and necrosis in longer perfusions.

Conclusion

We observed significant liver damage and impaired metabolic function during extended NMP in grafts after prolonged warm ischemia. While we hypothesized an association between higher donor age and increased susceptibility to ischemia-reperfusion injury, our study did not show greater damage in grafts from elderly donors. Further research into age-related differences in inflammatory pathways and regulatory mechanisms is needed, particularly regarding the potential of NMP to improve quality of elderly donor livers.

References

[1] Renz, J.F., et al., *Utilization of extended donor criteria liver allografts maximizes donor use and patient access to liver transplantation.* Ann Surg, 2005. **242**(4): p. 556-63; discussion 563-5.
[2] de Vera, M.E., et al., *Liver transplantation using donation after cardiac death donors: long-term follow-up from a single center.* Am J Transplant, 2009. **9**(4): p. 773-81.
[3] Michelotto, J., et al., *Ex vivo machine perfusion: current applications and future directions in liver transplantation.* Langenbecks Arch Surg, 2021. **406**(1): p. 39-54.
[4] Rodriguez, R.P., et al., *Outcome of Liver Transplants Using Donors After Cardiac Death With Normothermic Regional Perfusion.* Transplant Proc, 2022. **54**(1): p. 37-40.
[5] Strobl, F., et al., *Advancing Perfusion Models: Dual-Vessel Ex Vivo Rat Liver Perfusion Based on a Clinical Setup.* Tissue Eng Part A, 2023. **29**(19-20): p. 518-528.

Poster Session 02: Immunology

PV02-01

Long-Term Renal Benefit Of A CNI-Sparing Regimen In A Biopsy-Guided Personalized Immunosuppression Program After Liver Transplantation

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Introduction
Side effects of chronic immunosuppression after liver transplantation (Ltx) are a source of high morbidity and mortality. Biopsy guided Personalization of immunosuppression (BGPIS) including CNI sparing regimen promises an improved balance of necessary control of alloreactivity and side effects [1].

Methods
In a single center retrospective study (10/2018 - 01/2024), rejection rates and kidney function were monitored longitudinally in participants grouped into those patients with CNI reduction compared to those without CNI reduction.

Results
253 liver transplant recipients in our BGPIS (at baseline biopsy: 52 years of age and 104 months after Ltx) were monitored for up to three follow-up visits (FU) after the initial surveillance biopsy (FU1: with/without CNI reduction n=79 &157 with median FU of 13 months; FU2: n=71 & 141 with median FU of 33 months; FU3: n=48 & 95 with a median FU of 46 months). At baseline biopsy patients with CNI reduction had a lower kidney function than patients without CNI reduction (eGFR: 61 ml/min vs 84 ml/min; p=0.01). However, longitudinally kidney function was stable in patients with reduced CNI regimen, while it was declining in those without CNI reduction (delta-eGFR from baseline to FU1: -0,5ml/min vs -2ml/min p=0.01; FU2: -1ml/min vs -5ml/min p<0.001; FU3: -1ml/min vs. -8 ml/min p=0.001). CNI trough levels were not significantly different between both groups at each follow-up. Additionally, rejection rates were not significantly different between the two groups at each FU (CNI reduction: 4%; no CNI reduction: 5% p=1).

Conclusion
CNI reduction can stabilize kidney function without increased rejection rates, while regimen without CNI reduction were associated with declining kidney function. Further subgroup and multivariate analysis are ongoing.

Reference
[1] Saunders EA, Engel B, Höfer A, Hartleben B, Vondran FWR, Richter N, Potthoff A, Zender S, Wedemeyer H, Jaeckel E, Taubert R. Outcome and safety of a surveillance biopsy guided personalized immunosuppression program after liver transplantation. Am J Transplant. 2022 Feb;22(2):519-531. doi: 10.1111/ajt.16817. Epub 2021 Sep 13. PMID: 34455702.

PV02-02

Transient Peripheral Chimerism In Lung Transplant Recipients Does Not Correlate With PGD But CLAD

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Introduction
For patients suffering from end-stage lung disease, lung transplantation (LTx) is the ultimate treatment option. Yet survival rates of LTx recipients compared to other SOT recipients are low due to the development of primary graft dysfunction (PGD) early after LTx, whereas long-term outcome is hampered by chronic allograft dysfunction (CLAD) resulting from poorly defined immune mechanisms.

Methods
Peripheral blood samples of n=97 lung recipients were analyzed at different time points before (pre), after (post), 24h and 3wks post-LTx for immune subset distributions by multicolor flow cytometry. Donor-derived passen-

ger leukocytes were stained in recipient blood (n=44) by HLA-allele specific antibodies and detected by FACS. Clinical parameters, i.e., PGD, CLAD, were recorded of all patients.

Results

We demonstrate dynamic changes with decreased T, B and NK cell subsets immediately after LTx with the strongest impact on memory $CD4^+$ and $CD8^+$ T cells, accompanied by a relative increase in NK cells. Donor-derived T/NK cells were detected in recipient blood immediately after LTx, persisting for three weeks and, thereby, creating a transient chimerism in recipient blood. These donor cells exhibited a $CD69^+$ but $CD103^-CD49a^-CD25^-$ phenotype, which was shared by T and NK cells in organ storage solutions. Moreover, these $CD69^+CD103^-CD49a^-$ TRM-like T/NK cells were also found in human explant lung tissue among other subsets and in preservation solutions. The presence of donor T and NK cells did not differ between patients without (grade 0-1) or with PGD grade 2-3, supporting the concept that PGD primarily results from ischemia/reperfusion injury. By contrast, higher frequencies of donor T cells within the first three weeks showed a tendency for protection from CLAD two years after transplantation though the correlation did not reach statistical significance.

Conclusion

To the best of our knowledge, we show for the first time that a transient chimerism is established within the first weeks after LTx by donor-lung derived T and NK cells, which does not correlate with PGD but may contribute to protection from CLAD development. Hence, donor T cells in recipient blood may have a long-term protective role in LTx.

PV02-03

The FcγIIIA Receptor 158 Gene Polymorphism Of The Natural Killer Cells Is Associated With Acute Humoral Rejection After Kidney Transplantation

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Introduction

Antibody-mediated rejection (ABMR) is a common cause of long-term kidney transplant loss. Exposure to alloantigens, including HLA, can lead to the production of donor-specific antibodies (DSA). The latter are directed against the HLA on the endothelium and can either lead to a complement-mediated inflammatory reaction or activate NK cells by FcγRIIIA receptor binding (ADCC, antibody-dependent cell-mediated cytotoxicity). The FcγRIIIA-V/V-158 genotype increases CD16-mediated NK cell cytotoxicity and is associated with higher glomerulitis, peritubular capillaritis (ptc) scores and injury responses. We investigated the association between FcγIIIA receptor 158 gene polymorphism and post-transplant outcome taking biopsy results into account.

Methods

This retrospective observational study included 492 kidney transplant patients who were studied at the University Hospital of Dresden on average 7.4 years (± SD 6.4 years, median 5.8 years) after kidney transplantation. Between June 2020/2021, the FcγRIIIA-158 genotype

was determined by RT-PCR (ThermoFisher®) and clinical data were retrospectively analyzed.

Results

The risk of acute ABMR was three times higher (7,8 % versus 25%) in rejecting recipients with genotype V/V-158 than in recipients with genotypes V/F and F/F-158, and there was a significant association between genotype V/V-158 and ABMR (p=0.038) as well as interstitial inflammation (p=0.035). No correlation was found between genotypes and chronic active ABMR, creatinine levels nor BANFF scores for glomerulitis, ptc or C4d positivity.

Conclusion

Our data suggest that the FcγRIIIA-V/V-158 genotype in NK cells is involved in acute ABMR after renal transplantation. Given the current trend of increasingly liberal definitions of unacceptable HLA antigens banned as donor HLA mismatch, FcγRIIIA-V/V-158 genotype determination may identify the cases that could benefit from stricter limitations. Future studies need to investigate its causal relationship to better elucidate the mechanisms of acute ABMR.

PV02-04

Comparison Of The Prognostic Value Of Three Different Single Antigen Tests

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Introduction

Single antigen (SA) tests are indispensable for HLA antibody identification. 3 tests are available, but little is known about their comparative prognostic value.

Methods

Sera from kidney transplant patients with preformed donor-specific antibodies (DSA) were selected from a multicenter study. All 49 sera with sufficient aliquots

were tested by a microspot SA test from BAG and bead array SA assays from Immucor/Werfen (IMM) and ThermoFisher/OneLambda (OLI). ABMR-free survival (ABMR-S) within 6 months and 10-year death-censored graft survival (10yGS) were evaluated according to (1) number of SA tests classifying the serum as DSA-positive (DSA+), and (2) number of SA tests detecting at least 1 identical DSA specificity.

Results

(1) 22 patients were DSA+ by all tests and had lowest ABMR-S and 10yGS. OLI was most sensitive and classified all sera as DSA+, that were DSA+ by BAG and/or IMM. It detected DSA in 14 sera which were DSA-negative (DSA-) by both BAG and IMM; however, these patients had similar ABMR-S and 10yGS as patients without any DSA. Overall, BAG and IMM had comparable sensitivity: 8 sera were DSA+ by BAG and OLI, and 5 sera DSA+ by IMM and OLI. Additional review revealed that some OLI results had been influenced by false positive reactions due to denatured beads or high background, while some weak reactions in the BAG test had been missed. Correction of these misinterpretations did not significantly change the above-mentioned results. (2) In 18 sera, at least 1 identical DSA was detected by all tests. These patients had worse ABMR-S and 10yGS. In 14 sera, the same DSA was detected by IMM and OLI, or by BAG and OLI, respectively. These patients had lower ABMR-S, but no significant difference in 10yGS. In 17 sera, DSA were detectable by 1 or more tests, but no specificity was positive in more than 1 assay (in all sera DSA were detected by OLI, in 1 additionally another DSA by IMM, and in 2 another DSA by BAG). ABMR-S and 10yGS were similar to DSA- patients.

Conclusion

OLI was most sensitive but also prone to false positive results. While false positive reactions were rare for BAG and IMM, these tests missed some DSA associated with an increased risk for ABMR.

The study was supported by free reagents provided by the companies BAG, Immucor and OneLambda/ThermoFisher.

PV02-05

The Taboo Concept 2.0: Homozygosity Of Any HLA Locus Is Associated With Dedicated HLA Antibody Patterns

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Introduction

In a collaborative study of the University Hospital Leipzig and the Charité Berlin on a large cohort of kidney transplant recipients, we aimed to analyse the occurrence of HLA-specific antibody patterns with respect to the HLA repertoire of the patients.

Methods

Patients typed for the relevant HLA determinants using next generation sequencing. Antibody screening was performed by multiplex-based technology using microspheres coupled with the HLA alleles of HLA class I and II.

Results

Patients homozygous for *HLA-A*02, HLA-A*03, HLA-A*24, HLA-B*07, HLA-B*18, HLA-B*35, HLA-B*44, HLA-C*03, HLA-C*04, HLA-C*07* for class I and for class II*: HLA-DRB1*01, HLA-DRB1*03, HLA-DRB1*07, HLA-DRB1*15, HLA-DQA1*01, HLA-DQA1*05, HLA-DQB1*02, HLA-DQB1*03(7), HLA-DQB1*06, HLA-DPA1*01,* and *HLA-DPB1*04* were found to have a significant higher antibody production compared to the heterozygous ones. All HLA determinants are affected. Remarkably, *HLA-A*24* homozygous patients can produce antibodies towards all HLA-A determinants, while HLA-B*18 homozygous make antibodies towards all HLA-B and selected HLA-A and -C antigens and are associated with an elevation of HLA-DRB1, partly -DQB1, and -DPB1 alleles. Homozygosity for the HLA class II *HLA-DRB1*01,* and *HLA-DRB1*15* seems to increase the risk for antibody

responses against most of the HLA class I antigens (HLA-A, -B and -C) in contrast to *HLA-DQB1*03(7)* where a lower risk towards few HLA-A, and B alleles is observed.

Conclusion

The widely observed differential antibody response is to be accounted to the patient's HLA repertoire. Homozygous patients are at risk to produce HLA-specific antibodies hampering the outcome of transplantation or any substitution. Including this information in the allocation procedure might reduce antibody mediated immune reactivity and prevent graft loss. In addition, all patients in need of HLA based substitution and being homozygous in any of the HLA loci should treated in a way to avoid sensitization.

PV02-06

Epitope Matching In Kidney Transplantation: Examples From The Living Cohort In Leipzig

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Introduction

Following transplantation, the production of donor-specific HLA antibodies (DSA) might cause humoral rejection followed by graft loss. We demonstrated the benefit of high-resolution HLA typing for the determination of these antibodies (Lehmann et al. doi: 10.3389/fimmu.2023.1094862).

Methods

Here, we present the use of 'epiTOol', an interactive tool for all-in-one processing of HLA typing/antibody data. We analyzed a cohort of 108 living transplants regarding their antibody verified epitopes matches (EM) and mismatches (EMM). The recipients were 59% related (43% 1st degree).

Results

For HLA class I, we found unique epitopes for HLA-A (n=33), -B (n=28) and -C (n=20), with **144KR** being the most frequently EMM (n=29). For HLA-class II, the highest number of different epitopes are observed for HLA-DR (n=37), followed by -DQ (n=28) and -DP (n=13). The EMM ranged from 0-50 (6-1 pairs respectively)-. The largest EMM was observed for the DR locus (n=522), followed by A (n=440), DQ (n=418), B (n=323), C (n=217) and DP (n=213). The number of EM is not proportional to the number of EMM. The DR locus has the most matched epitopes n=1736, followed by DQ (n=1307), A (n=1183), B (n=888), C (n=798) and DP (n= 663). Finally, via epiTOol we mapped the "antibody epitopes" (donor specific epitopes). Interestingly, 33% (n=36) of the recipients have not formed anti-HLA antibodies following kidney transplantation although up to 40 epitope mismatches were present. In contrast, recipients with only nine EMM had produced antibodies towards the donor.

Conclusion

In conclusion, the number of EMM in a transplant is not important but the type of EMM. Defining deleterious epitopes for the patient is a step in the good direction, to establish an epitope matching in postmortal transplantation.

PV02-07

Acute COVID-19 Is Associated With Altered CD8 T-Cells Indicative Of Impaired Ability To Control Epstein-Barr Virus Reactivation

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Introduction
Patients undergoing kidney transplantation and subsequent immunosuppressive therapy are at heightened risk for viral reactivation and associated complications. The COVID-19 pandemic has brought renewed attention to this issue, as emerging evidence suggests a link between SARS-CoV-2 infection and reactivation of latent viruses like Epstein-Barr virus (EBV). Uncontrolled viral reactivation in immunocompromised transplant recipients can have severe consequences, such as graft rejection and other organ dysfunction.

Methods
In this study, we evaluated reactivation of latent EBV in COVID-19 patients during the first pandemic wave using biobanked samples. We assessed all major immune cell populations by flow cytometry in a cohort of 61 patients with moderate to critical COVID-19 at the time of hospitalization. Additional blood samples from these patients were biobanked for later analysis. Using these biobanked samples, we evaluated the co-occurrence of CMV, EBV, as well as HHV-6A and -6B by qPCR.

Results
EBV reactivation was observed in patients with critical or severe COVID-19 (24/33 patients; 72.72%) as well as those with moderate disease (19/28; 67.86%) at the time of hospital admission. In contrast, CMV and HHV-6A and -6B only occurred in low frequency (0-15.15%). In COVID-19 patients with EBV reactivation, the degree of expression of the T-cell co-stimulatory CD28 and co-expression of CD28 and the integrin CD11a was diminished on CD8 T-cells. In contrast, the frequency of CD8 T-cells expressing the proliferative exhaustion marker CD57 was increased.

Conclusion
Collectively, these data point to an altered activation phenotype of circulating CD8 T cells and that higher replicative senescence is associated with EBV reactivation. The data suggest an impaired ability of the CD8 T-cell compartment to control EBV reactivation in COVID-19 patients.

PV02-08

Bcl6 Inhibitors – A Novel Immunosuppressive Strategy Disrupting T-B Collaboration In Alloimmune Responses

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Introduction
The transcription factor (TF) Bcl6 is critical for T follicular helper cells (Tfh) and germinal center B cells, which collaborate in humoral alloresponses. We used a novel model of Tfh differentiation to test the immunosuppressive effects of Bcl6 inhibitors (Bcl6i).

Methods
To simulate Tfh differentiation, we cocultured naïve T cells (Tn) with CPG-activated B cells (allo BC) from healthy donors (n=6) for 6 days. T cell proliferation, Tfh and B cell markers, and T and B cell Bcl6 expression were measured by flow cytometry. In addition, Bcl6i (FX1 12.5, 3.125 and 0.78 ug/ml), Belatacept (Bela, 10 and 5 ug/ml), or Tacrolimus (Tac, 10 or 5 ng/ml) were added to cocultures (n=5). The effects of Bcl6i on gene expression was measured in CD3/CD28 stimulated Tn by qPCR (n=8). Bcl6 expression was analysed in kidney transplant (Ktx) biopsies (7 TCMR, 3 ABMR/TCMR, 10 non-rejection) using multiplex immunofluorescence in situ hybridization.

Results

Allo BC potently stimulated T cell proliferation (0.6% vs 47%, p=0.0025) and expression of Tfh markers CXCR5 (p=0.014), PD-1 (p=0.015) and ICOS (p=0.12). CD4+CXCR5+PD-1+ Tfh-like cells increased from 0.2% to 30.8% (p=0.032) and showed increased Bcl6 expression (vs. CD4+CXCR5-PD-1- cells, p=0.031). Furthermore, cocultured allo BC upregulated Bcl6 expression (p=0.013) and differentiated into a memory phenotype (IgD+CD27+/IgD-CD27+)(p=0.005, vs. allo BC alone). Using this model of B cell-dependent Tfh differentiation, we found that both FX1 and Tac significantly inhibited expression of T cell activation markers CD45RO (FX1 p=0.0003; Tac p<0.0001), PD-1 (FX1 p=0.051; Tac p<0.0001), and ICOS (FX1 p=0.028; Tac p=0.0003), while Bela moderately inhibited ICOS expression (p=0.034), but not other markers. Furthermore, TCF-1 and ASCL2, two TF upstream of Bcl6 during Tfh differentiation, were significantly upregulated by Bcl6i. Preliminary analyses showed increased Bcl6 expressing CD4+ cells in biopsies with ABMR/TCMR compared to TCMR (p=0.027) or no rejection (p=0.011).

Conclusion

Our study highlights T-B collaboration as an important mechanism of T and B cell activation, which can effectively be ininhibited by Bcl6i as a novel strategy against humoral allosensitization.

PV02-09

Surface Molecule Expression Of Kidney Tubular Epithelial Cell Derived Extracellular Vesicles – A New Perspective On The Modulation Of Alloimmunity?

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Introduction

Alloimmunity is one of the leading causes of a limited short- and long-term graft survival. Extracellular vesicles (EVs) have recently been recognized to hold a key role in immune processes in many conditions. They could therefore also impact alloimmunity, for example through the expression of surface proteins that in- or decrease adaptive immune cell reactivity after inflammatory or hypoxic episodes. Kidney parenchymal cells are an important source of EVs in kidney transplantation. Thus, we aimed to shed light on the immunomodulatory molecule expression of renal tubular epithelial cells (rTECs) derived EVs in thepathophysiology of alloreactivity.

Methods

rTECs of healthy probands and kidney transplant patients were isolated from urine using a protocol established by our group. We compared different immunomodulatory cytokines (IL1β, IFNγ, TNFα, IL6, IL17A, and IL22) regarding their impact on EV-production and EV surface marker expression. EVs were isolated from cell-culture supernatants by ultracentrifugation. Quantity, size distribution, and typical morphology were analyzed by nanoparticle tracking analysis, BSA assay and electron microscopy. Surface expression of tetraspanins, MHC and immunomodulatory molecules such as PDL-1, ICAM-1, and ICOS-L was analyzed by flow cytometry. Finally, functional impact of EV incubation on T cell activation was studied.

Results

IL1β stimulation was observed to enhance vesicle production strongest. Surprisingly, IFNγ and TNFα only moderately increased the quantity of EVs, despite their regular use as EV-production stimulants. Furthermore, we could show that rTEC – Evs express immunomodulatory molecules to varying degrees depending on what cytokine was used for stimulation. Consequently, T cell activation upon TCR stimulation in coculture with rTEC-EVs was impacted, implying a context-dependent mechanism of immune alteration.

Conclusion

Taken together, we showed that rTECs can have immunomodulatory effects via the production of EVs, leading to new insights into alloimmunity after ischemia-reperfusion injury and intragraft inflammation

PV02-10

Alloreactive Memory CD4+ T Cells Respond To Kidney Parenchymal Cells Without Help Of Professional Antigen Presenting Cells

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Introduction

Alloreactive CD4+ T cells are involved in different types of allograft rejection. Direct allorecognition is regarded to be dependent on professional antigen presenting cells (APC), the main presenters of MHC-II molecules and co-stimulatory molecules. Thus, a common notion is that this pathway becomes insignificant after the disappearance of the donor's APCs. We and others demonstrated expression of MHC-II on kidney tubular epithelial cells (TECs) and their potential role as APCs in the alloimmune context after kidney transplantation. Thus, we were interested to further study the potential of TECs to directly stimulate CD4+ T cells.

Methods

Using a protocol established in our group, we isolated TECs of healthy probands and kidney transplant patients from urine. After stimulating the TECs with IFN**γ**, TNF**γ**, and IL-1**γ** for 24h, we co-cultured them with either PBMC or isolated T cells from another donor in the presence or absence of HLA-blocking antibodies. After 24h we analyzed the cells using a 15 color flow cytometry panel.

Results

Remarkably, CD4+ and CD8+ T cell activation in PBMC samples containing APCs and in T cell isolated samples after coculture with allogeneic TEC was identical. Thus, TEC seem to be capable of stimulating CD4+ and CD8+ T cells even in absence of professional APCs. Of interest, this stimulation was MHC-I and -II dependent, since MHC-blocking antibodies significantly diminished activation. Similarly, stimulation was significantly reduced when TEC were not stimulated with cytokines prior to co-culture. The activated CD4+ T cells were predominantly TH17 cells and had an effector or central memory phenotype, pointing towards previous priming in vivo. This ratio shifted towards an effector memory phenotype in the samples without professional APCs.

Conclusion

We showed that TECs are capable of direct T cell activation, also in absence of professional APCs. The most abundant cell type of the kidney therefore potentially has an important role in immunological processes such as acute or chronic rejection in transplanted patients and could be an important key to diagnostic or therapeutic interventions. Future studies might investigate this role and influencing factors further.

PV02-11

Immune Checkpoint Inhibitors In Post-Liver Transplant Of Hepatocellular Carcinoma

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Introduction

Hepatocellular carcinoma (HCC) treatment strategies, guided by the BCLC-staging system, form a heterogenous landscape. HCC can be cured with resection

or liver transplant (LT) but the incidence of recurrence (up to 20%) remains a significant challenge. Immune checkpoint inhibitors (ICI) have reshaped the therapy of advanced stage HCC. But ICIs in the setting of LT pose a risk of rejection and hold unclear benefit in both the pre- and post-transplant salvage setting. In the post-LT setting, there are few treatment options if there is a recurrence of disease, which forces treatment teams to reconsider checkpoint inhibitors. Case reports of patients treated with ICIs post-transplant utilized either the PD-1 inhibitors nivolumab or pembrolizumab. The PDL-1 inhibitors are new treatment option for there are only a hand-full reported cases using this combination in the post-LT setting. The significant barrier to ICI in the transplant setting is the potentially disastrous consequence of organ rejection.

Methods

In this retrospective chart review, we demonstrate an additional patient who received ICI in the post-LT setting. The 69a male with HCV cirrhosis was diagnosed with HCC. He underwent TACE followed by LT in 2020. Immunosuppression included tacrolimus, mycophenolate and prednisone. Explant was notable for 3 viable tumors. 18 months after LT he was found to have recurrence of disease. He was treated with 3 times TACE but had disease progression. He was then treated with atezolizumab/bevacizumab in an individual therapy attempt. Therapy is still ongoing up to now.

Results

Till now, now no rejection was observed and the patient is still in remission.

Conclusion

Post-liver transplantation disease recurrence remains challenging, requiring a balance between effective therapy and preserving graft function. Emphasis should be placed on clinical trials validating the risk-benefit ratio of ICIs for liver transplantation, guiding appropriate patients' selection, and establishing clear management pathways. Further studies should evaluate PD-L1 status of grafts and the effect of ICI on the balance of immune regulators, such as CD8+ T cells and regulatory T cells (Tregs).

PV02-12

Influence Of Post-Transplant Diabetes Mellitus On Inflammation And BKV, CMV And EBV Reactivation In Kidney Transplant Patients

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Introduction

The development of post-transplant diabetes mellitus (PTDM) is a frequent metabolic complication affecting 20-30% of patients and increases the risk for cardio vascular events as well as for various infections. Most patients develop an early PTDM within 3-6 months post-transplant with a reversibility rate of 20-30% during the first 24 months. Several risk factors including calcineurin inhibitor (CNI) and glucocorticoid treatments as well as inflammation have been identified. Infections and reactivation of latent viruses are known to provide systemic inflammation. The aim of this study was to analyze the role of reactivation of latent viruses such as BKV, CMV and EBV, pro-inflammatory cytokines and regulatory genes for *de novo* PTDM (dnPTDM) development in kidney transplant patients during the first post-transplant year.

Methods

540 kidney transplant patients were monitored at 8 visits during the first year post-transplant. Blood samples were

collected and analyzed for BKV, CMV and EBV viral loads. A pro-inflammatory cytokine panel and the expression of B cell regulating genes were analyzed in parallel. Graft function, defined by eGFR, was also analyzed.

Results

In total, 76 patients were identified with dnPTDM (defined as pre-transplant HbA1c < 5.7%, post-transplant HbA1c > 6.5%) in comparison to 290 non-diabetes patients (controls). BKV, CMV and EBV $viral_{max}$ loads showed no differences between dnPTDM and controls. There was also no difference in the proportion of patients with elevated (> 2,000 cp/ml) or high (> 10,000 cp/ml) viral loads. Interestingly, a significant downregulation in the gene expression of FCRL2 and MS4A1 in combination with higher levels of inflammatory cytokines including IL-6 were detectable in dnPTDM patients.

Conclusion

Reactivation of BKV, CMV or EBV was not associated with dnPTDM development. Nevertheless, our data suggest a higher pro-inflammatory milieu in dnPTDM patients indicated by higher pro-inflammatory cytokine expression and reduced expression of regulatory B cell genes.

PV02-13

Tubular Epithelial Cells Can Modulate Adaptive Immune Responses Upon Proinflammatory And TLR3 Stimulation By Production Of APC Cytokines And Surface Molecules

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Introduction

Emerging evidence suggests an immunomodulatory function for tubular epithelial cells (TECs), comprising the majority of the kidney parenchyma. Conventionally, professional APCs are considered the primary source of cytokines and co-stimulatory or -inhibitory molecules crucial for directing T cell activation and differentiation. We aimed to investigate how TECs might influence the adaptive immune response under scenarios of inflammation as well as viral and bacterial threat.

Methods

Previously, we demonstrated that renal TECs can be cultivated from the urine. We stimulated the primary TEC with proinflammatory cytokines (10ng/ml interferon ϕ, 20ng/ml tumor necrosis factor α, 10ng/ml interleukin 1β), TLR-3-Agonist Poly I:C (250 ng/ml), and TLR-4-Agonist lipopolysaccharide (LPS, 2 µg/ml) for 24h. Cell culture supernatants were measured by flow cytometry based multiplex assay, and cells stained for flow cytometric analysis comprising over 20 markers.

Results

TECs produced a diverse set of cytokines upon proinflammatory stimulation and to a lesser extent after Poly I:C stimulation, but not LPS. Interestingly, TECs also produced cytokines associated with T helper cell differentiation and NK stimulation. IL12p70 promotes TH1 cell differentiation and stimulates NK-cell activation and proliferation. Production by TECs was significantly upregulated upon proinflammatory stimulation. IL33 is associated with promoting type 2 immune responses and was significantly elevated after proinflammatory treatment and poly I:C stimulation. Similarly, IL-23, a cytokine involved in differentiation and maintenance of TH17-cells, was produced by TECs upon proinflammatory treatment. Interestingly, TECs also expressed immune-activators CD40, ICAM, ICOS-ligand, as well as immunomodulatory HVEM and PDL1 under inflammatory conditions.

Conclusion

Taken together, we found evidence that TECs could influence the activity and phenotypes of infiltrating T cells and NK cells. Given their high number in the kidney, this might be of relevance in intrarenal infections, autoimmune diseases, and kidney transplantation. Further experiments will need to verify and attempt to quantify the influence of TEC on adaptive immune responses.

PV02-14

Vaccination Status In Organ Transplant Recipients – Status Quo Analysis In A Monocentric Study

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Introduction

Solid organ transplantation (SOT) patients are at an increased risk of infection. Consequently, infection prevention measures are of paramount importance. While vaccination is the most effective method of preventing infectious diseases, the vaccination rate among SOT patients remains low. This study aimed to survey the vaccination rate of outpatient SOT patients and gain insight into the factors influencing vaccination hesitancy.

Methods

After ethical approval was obtained and written informed consent was provided by all participants the vaccination rate was determined by examining the vaccination certificates. The evaluation was based on the recommendations of the Robert-Koch-Institute (RKI) for the vaccination of SOT patients. The vaccines were categorised into three groups: standard vaccines, indicated vaccines for SOT patients and additional vaccines for a certain gender, age or risk group. In an interview, SOT patients were asked to rate statements on beliefs and knowledge about vaccination. Statistical analyses were performed using chi-square tests and Spearman-Rho correlation.

Results

A total of 126 patients (mean age 58.7 $\pm$13.8 years, 42.1% female) were included in the analysis. The cohort comprised 55.5% liver transplantations (LTX), 38.1% kidney transplantations (NTX), 3.2% pancreas-kidney transplantation and 3.2% of other combined transplantations. The mean time after the transplantation was 101 months ($\pm$96 months). For 115 patients (91.3%), a valid vaccination certificate was available. Of the 115 patients, 64.3% were up to date with standard vaccines. Only one patient (0.9%) had received all indicated vaccines. At least one additional vaccine was received by 49.6% (N=57) of the study population. The vaccination rate against hepatitis B among NTX patients is 88.1%, which is significantly higher than the 55.4% rate among LTX patients (X^2=13.7, p<0.001, N=107). There was a significant correlation between trust in vaccinations and willingness to get vaccinated in the future (r=0.362, p<0.001, N=123).

Conclusion

The proportion of the population vaccinated remains low, indicating a need for action to improve trust and encourage individuals to maintain up-to-date vaccination status.

PV02-15

Stationary Treatment Outcomes Of Kidney Transplanted Patients With Infectious Diseases According To Sex

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Introduction
Kidney transplantation (KT) is the established therapy in end-stage renal failure. Infectious diseases are a widespread comorbidity after KT which influences survival. However, sex plays a part at different levels of transplantation. Regarding patients with KT only few studies have focused on the differences that may occur in infectious diseases outcomes according to sex.

Methods
We included 87 men (54.38%) and 73 women (45.62%) with KT (>18 years of age) admitted in the Infectiology department of the University Hospital Essen from March 2016 to October 2017. Data was obtained from patients' electronic files or in a phone interview. Analyses were done in R. Significance testing for sex differences was done with chi-square tests for categorical data and independent t-tests for continuous data. Significance testing for factors affecting hospital length of stay (LOS) was carried out using univariate and multivariate linear regression models in combination with type III ANOVA. We included all variables that were both significantly different between the sexes and had a significant effect on LOS in our multivariate model.

Results
The main reason for admission in both groups was a gastrointestinal infection (29.9% of men, 34.2% of women, p=0.675), followed by a urinary tract infection (21.8% of men, 32.9% of women, p=0.165). Patients' LOS came to 7.71 (±5.87) days for men and 10.97 (±9.09) days for women (p=0.007). Factors that were significantly associated with both sex and LOS were hemoglobin-levels (0.675±0.26, p=0.01) and use of diuretics (2.333±1.176, p=0.049). When adjusted for these covariates, there was no significant association between sex and LOS (2.185 ±1.199, p=0.07). No significant difference was found in the three-month mortality according to sex, as 4 (4.6%) men and 4 (5.5%) women with KT were deceased (p=1).

Conclusion
In summary, the results of our patient cohort suggest, that infectious diseases and outcome in patients with KT are not influenced by sex.

PV02-16

Distinct Characteristics And Outcomes Of Invasive Fungal Infections In A Large Renal Transplant Cohort: Results Of The DZIF Transplant Cohort Study

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Introduction
Pneumocystis jirovecii pneumonia (PjP) and Aspergillosis represent both life-threatening fungal infections seen in renal transplant recipients, but they may differ in their characteristics and outcomes.

Methods
As part of the Transplant Cohort Study led by the German Center for Infection Research (DZIF), we assessed cases of Aspergillosis and PjP in adult participants who underwent renal transplantation at our local center in Heidelberg between 11/2012 and 03/2024.

Results
Among 604 recipients (63% male, mean age 49±14 years), we identified 11 cases of invasive Aspergillosis (10 pneumonia cases, one rhino-sinusal aspergilloma) and 7 cases of PjP. Shared characteristics included male gender (80%), older age (60±10 years), and deceased donor grafts (87%). The majority of PjP cases occurred after the first year (71%), with a median prophylaxis duration of 184 days. Most patients had prior CMV infections (56%), multiple hospitalizations (mean=4) and an intensified immunosuppression (57%). Two experienced combined pneumonia, with HSV-1 or CMV co-isolations. All PjP patients presented with persistent cough, subfebrile temperatures, and elevated infection parameters upon admission. Complications included infection- or therapy-related graft function decline (71%) and one case of graft failure. No PjP-related deaths were recorded.

Aspergillosis occurred earlier post-transplantation (59% within 3 months) and presented with more subtle initial symptoms, primarily fatigue and dyspnea. Cough was absent in 80% of pneumonia cases. Complications included graft function decline (64%), respiratory insufficiency requiring mechanical ventilation (40%), sepsis (25%), graft (18%) and liver failure (18%), progressing rapidly. The mortality rate was 50%, involving septic dissemination, respiratory failure and meningitis with a mycotic basilar artery aneurysm.

Conclusion
Both Aspergillosis and PjP presented with nonspecific initial symptoms and were more common in older recipients of deceased donor grafts. Aspergillosis occurred earlier post-transplantation, with subtler symptoms and higher mortality. Early diagnosis is crucial for saving recipients' lives and grafts, as both conditions can progress rapidly.

Poster Session 03: Kidney Rejection Immunosuppression

PV03-01

Subtherapeutic Tacrolimus Target Trough Levels In The First Ten Days After Kidney Transplantation Correlate With Increased Rejection Rates

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Introduction
The calcineurin inhibitor tacrolimus is used as a first-line immunosuppressant after kidney transplantation in combination with an antiproliferative agent and steroids. The drug has a narrow therapeutic window, but achieving and maintaining the target trough level range is complicated by inter- and intrapersonal variability in tacrolimus metabolism. Given that the rate of rejection is highest within the first year after transplantation, the question arises as to whether delayed reaching of the tacrolimus trough target range after transplantation is associated with an increased risk of rejection.

Methods
In a retrospective approach, we analyzed the data of 664 adult patients who received a kidney transplant at the University Hospital of Münster between January 2007 and December 2018. Induction therapy was performed

with either antithymocyte globulin, alemtuzumab or basiliximab. Tacrolimus, a mycophenolate derivative and prednisolone were used as initial immunosuppression. The incidence of histologically confirmed rejection within the first and first five years after transplantation and tacrolimus trough levels from day 1 to day 10 after transplantation were analyzed.

Results

An increased proportional number of days with tacrolimus trough levels below the target range (8-10 ng/ml) correlated positively with the occurrence of histologically confirmed graft rejection within one year (Odd's ratio (OR) 2.22, 95% confidence interval (CI) 1.12-4.4) and five years after transplantation (OR 2.81, 95% CI 1.28-6.14). Accordingly, an increased proportional number of days with tacrolimus trough levels above the target range was associated with a lower number of rejections within one (OR 0.37, 95% CI 0.16-0.88) and five years (OR 0.26, 95% CI 0.1-0.68) after transplantation. The rate of rejection did not correlate with the induction therapy used (within one year after transplantation: p=0.58 and within five years after transplantation: p=0.6).

Conclusion

These results suggest that rapid achievement of tacrolimus target levels after transplantation is important with regard to the occurrence of post-transplant graft rejection. Patients with rapid tacrolimus metabolism may be particularly at risk.

PV03-02

Urinary Metabolite Constellation Also Detects Very Early Post-Transplant Rejection In Living Donor Kidney Recipients

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Introduction

Kidney transplantation is the preferred treatment for end stage kidney disease, offering improved survival rates and quality of life compared to dialysis. However, acute allograft rejection remains a significant complication, necessitating accurate diagnosis for timely intervention. Standard serum creatinine monitoring lacks specificity, leading to unnecessary biopsies and missed subclinical rejection. Previously we published a novel metabolom-based urinary non-invasive test for the detection of renal renal allograft rejection (Banas M et al. EBioMedicine, 2019).

Methods

In this study, conducted as part of the UMBRELLA study, n=682 urine samples from 109 transplant recipients were analyzed using a recently introduced urine metabolite constellation of alanine, citrate, lactate, and urea. Parameters (n=29) such as induction therapy, warm ischemia time, and donor type were examined for their impact on the test's performance to identify biopsy confirmed rejection in the first 14 days post-transplant.

Results

Univariate analysis identified 10 significant confounders, particularly the influence of deceased organ donation on metabolic urine profiles. Multivariate analysis confirmed the relevance of parameters related to living donation and highlighted warm ischemia time as an independent factor affecting metabolite profiles. Subgroup analysis directly testing the performance of the rejection score revealed living donor recipients as the most accurately discriminated subgroup with an AUC of 0.720 (95% CI 0.62-0.82), followed by those with short (<30 min) warm ischemia times 0.702 (95% CI 0.61-0.79). Clinical observations supported these findings, with anomalies in the urine metabolite test often correlating with clinical complications.

Conclusion

The study underscores the importance of considering donor type and ischemia times when interpreting metabolomics data for rejection monitoring in kidney transplant recipients. Understanding these factors could enhance the accuracy of non-invasive rejection detection methods, facilitating timely intervention and improving patient outcomes.

PV03-03

SGLT2-Inhibition In Renal Transplant Patients Results In Beneficial Metabolic Effect But Not Reduction In Albuminuria

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Introduction
Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have been shown to slow the progression of CKD and reduce proteinuria in different patient cohorts. However, there is a lack of data on the use of SGLT2i in kidney transplant patients.

Methods
Data from 114 renal transplant patients, including 74 diabetic and 40 non-diabetic patients prescribed SGLT2i, were retrospectively analyzed at six months and one year after treatment initiation. Outcome measures evaluated included eGFR (CKD-EPI formula), albumin-to-creatinine ratio (ACR), body mass index (BMI), HbA1c, blood pressure, and safety parameters.

Results
After exclusion of 10 patients with chronic active antibody-mediated rejection ACR increased slightly by 17.23% ($p = 0.081$) at six months and by 14.5% ($p = 0.134$) at one year. This remains unchanged in the overall patient population ($p = 0,099$ and $p = 0,451$, respectively) or when non-diabetic patients are excluded ($p = 0,201$ and $p = 0,338$, respectively). eGFR decreased by 2.38 mL/min/1.73m² after six months and by 3.02 mL/min/1.73m² after one year (both $p < 0.05$). There was no change in blood pressure. Notably, reductions in mean BMI were observed in diabetic patients at 6 months (-0.269 kg/m², $p = 0.026$) and 1 year (-0.658 kg/m², $p < 0.001$), as well as in the overall patient population at 6 months (-0.235, $p = 0.018$) and 1 year (-0.464, $p < 0.001$). HbA1c decreased slightly at one year. There were four cases of urogenital infections without complications during the follow-up period. SGLT2i treatment was stopped in three patients due to an increase in serum creatinine, recurrent urogenital infections and other causes of acute graft injury.

Conclusion
ACR in kidney transplant recipients increased and eGFR decreased upon treatment with SGLT2i at 6 months and 1 year. As there is no control group, we cannot say in this study how these parameters would have developed without SGLT2i. Reductions in mean BMI and HbA1c suggest a favorable metabolic effect. In general, SGLT2i therapy was safe with minimal adverse events.

PV03-05

TCMR-Induced Epithelial Injury Patterns In Kidney Transplants

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ESOT

Introduction
Acute T-cell mediated rejection (TCMR) is a major challenge after kidney transplantation, posing risks to long-term allograft outcomes. Previous research highlighted the critical role of TCMR-induced renal epithelial injury, but the cellular origins and associated gene expression profiles remain poorly understood.

Methods
To study the molecular changes, we used C57BL/6 and BALB/c mouse models for allogeneic kidney transplantation and syngeneic controls. We analyzed the renal gene expression during TCMR by applying single nucleus RNA sequencing (snRNA-seq) and spatial transcriptomics on allogeneic and syngeneic kidneys 7 days post-transplantation. Differentially expressed genes and a gene set predictive of allograft outcomes were investigated per cell type, and results were compared to snRNA-seq data from human TCMR kidney biopsies and stable allografts without rejection.

Results
Mouse kidneys from allogeneic transplantation showed all histological hallmarks of TCMR. SnRNA-seq revealed a strong gene expression response, especially in C57BL/6 kidneys transplanted into BALB/c mice. These responses were most pronounced in kidney epithelial cells, particularly in the proximal tubules (PT) and thick ascending limbs (TAL), inducing distinct injury-associated cell states. Spatial transcriptomics identified a heterogeneous spatial distribution of these cell states between cortex and medulla. Published genes indicative of allograft outcome were mostly expressed in injured PT and TAL but showed heterogeneous differential expression in the different injured PT and TAL cell states. Cross-species analysis revealed a substantial overlap of differential gene expression and injured epithelial cell states between mouse and human TCMR.

Conclusion
Our study offers a detailed exploration of cell type-specific gene expression changes during TCMR in human and mice. The analysis of allograft outcome-associated genes revealed their origin from various injured epithelial cell states. This insight may help in identifying injured cell states most responsible for reduced graft function, potentially enabling targeted therapeutic interventions.

PV03-07

First Interim Results From The Protection Of Renal Function After Conversion Of Fast IR-Tac Metabolizers To Envarsus® Study (The Protect RENvarsus Study)

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Introduction
As shown in a retrospective single-center trial, renal function of fast immediate-release tacrolimus (IR-Tac) metabolizers can improve after conversion to once-daily LCP-tacrolimus (LCPT), whereas slow Tac metabolizers showed no differences over a follow-up period of 36 months [1]. This study was conducted to test this hypothesis in a multicenter trial.

Methods

In this multicenter European study, we aim to enroll 300 patients after renal transplantation (RTx). All RTx recipients had been converted from IR-Tac to LCPT one month or later after transplantation. Tac metabolism type was defined by calculation of the C/D ratio at one month after RTx: fast IR-Tac metabolizers (<1 ng/mL*1/mg) and slow (≥1) [2]. Renal function, acute rejections, infections, and survival rates were assessed in a 5-year follow-up.

Results

Meanwhile, preliminary data confirm that fast metabolizers who were switched to LCPT at a median time of 2.0 months after RTx (range: 1.0-253.1 months) showed a recovery of renal function. In contrast, slow metabolizers showed a constant eGFR after conversion to LCPT at a median time of 13.2 months (range: 1.2-172.8 months) after RTx. The rate of complications was low and comparable in both groups.

Conclusion

Early conversion to LCPT can be beneficial for fast IR-Tac metabolizers in terms of renal allograft function. Low complication rates in both metabolizer groups were confirmed in a 5-year follow-up.

References

[1] Thölking, G, Tosun-Koc, F, Jehn, U, et al. 2022, Improved Kidney Allograft Function after Early Conversion of Fast IR-Tac Metabolizers to LCP-Tac, J Clin Med, 11(5)

[2] Thölking, G, Schmidt, C, Koch, R, et al. 2016, Influence of tacrolimus metabolism rate on BKV infection after kidney transplantation, Sci Rep, 6: 32273

PV03-08

Age-Related Differences In Rejection Rates, Infections And Tacrolimus Exposure In Pediatric Kidney Transplant Recipients – A Benchmark Study Of The CERTAIN Registry

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Introduction

Data on age-related differences in rejection rates, infectious episodes and tacrolimus exposure in pediatric kidney transplant recipients (pKTR) on a uniform tacrolimus-based immunosuppressive regimen are scarce.

Methods

We therefore performed a retrospective analysis of 802 pKTR from the CERTAIN registry from 40 centers in 14 countries. Inclusion criteria were a tacrolimus-based immunosuppressive regimen and at least two years of follow-up. Patients were divided into three age groups (infants <6 years, school-aged children 6-12 years, and adolescents >12 years) to assess age-related outcomes. Data analyzed included demographics, immunosuppression, tacrolimus exposure, allograft function, biopsy-proven rejection episodes, and prevalence and type of infections.

Results

The mean age at transplantation was 11.2 ± 5.1 years, and 31.2% of patients received a living donor transplant. Besides tacrolimus, the most common immunosuppres-

sive drugs at year 1 post- transplant were MMF (77.8%) and glucocorticoids (82.8%). During the first 2 years post-transplant, infants had a significantly higher incidence of infections (P<0.001), and a significantly higher number of cumulative hospital days (P<0.001). Cox regression analysis showed a significantly lower risk of infection in adolescents, with a hazard ratio (HR) of 0.54 (95% CI, 0.43-0.66, P<0.001). On the other hand, adolescents had significantly higher rejection rates (P=0.032) than school-aged children and infants with an HR of 1.53 (95% CI 1.10-2.13, P=0.01). Infants had significantly lower tacrolimus trough levels, lower body surface area-corrected tacrolimus concentration-to-dose (C/D) ratios as an approximation of higher tacrolimus clearance, and increased tacrolimus intrapatient variability (P<0.002).

Conclusion

This is the largest study to date on the outcome of a tacrolimus-based immunosuppressive therapy in pKTR and highlights important age-related differences in rejection rates, infection episodes and tacrolimus exposure. Based on these findings immunosuppressive therapy in pKTR should be tailored according to the age-specific risk profiles of this vulnerable, but heterogeneous patient population.

PV03-09

The PRISMA Trial – Exploring The Role Of The Gut Microbiome In Personalised Immunosuppressive Therapy In Kidney Transplant Recipients

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Introduction

Potent immunosuppressive drugs such as tacrolimus (Tac) have improved clinical outcomes in kidney transplant (KT) recipients. However, patients suffer from serious adverse events due to over- or under-exposure. Known modulators of Tac exposure explain only a fraction of the inter-patient variability. Increasing evidence suggests that the metabolism of Tac by gut bacteria contributes to this variability. The objective of this research project is to identify gut microbiome-based features to better predict tacrolimus exposure.

Methods

PRISMA is a multicenter, prospective, longitudinal clinical study of de novo KT recipients. Stool samples were collected at defined time points before and within the first six months after transplantation and analyzed by metagenomic sequencing. The results were correlated with the Tac concentration/dose ratio (C/D ratio). Known factors influencing Tac pharmacokinetics, such as clinical, pharmacogenetic and demographic parameters were taken into account. Patients were recruited from the University Children's Hospital Heidelberg, the Department of Nephrology at the University Hospital Heidelberg and the Department of Nephrology at the University Hospital Münster.

Results

We report the results of an interim analysis of the PRISMA study including 30 patients with a longitudinal follow-up of 6 months post-transplant. We show that the integration of clinical and microbial characteristics improves the prediction of the Tac C/D ratio. In particular, it is possible to associate interpatient differences in the abundance of specific bacterial genera with interpatient variations in the Tac C/D ratio. In vitro validation of the identified genera suggests bacterial biotransformation of Tac to an inactive metabolite as a possible underlying mechanism.

Conclusion
Our preliminary results suggest a potential paradigm shift in our understanding of Tac exposure. It highlights the gut microbiome as a novel tool for personalized immunosuppressive therapy.

PV03-10

Molecular Rejection Phenotype Scores Predict Kidney Allograft Loss And eGFR Decline Along The AMR Continuum

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Introduction
The 2022 Banff Meeting Report suggests that biopsy-based transcripts related to antibody-mediated rejection (AMR) could substitute for microvascular inflammation (MVI). However, the new subgroups of AMR, DSA-negative MVI, and probable AMR need more outcome studies when molecular transcripts are used in the clinic.

Methods
We examined 297 kidney transplant biopsies by histology and the Molecular Microscope Diagnostic System (MMDx) from 2018 to 2023. Histologic findings were grouped into (1) probable AMR (n=53), (2) DSA-negative C4d-negative MVI (n=42), (3) AMR (n=71), and no AMR (n=131). Groups were further divided into molecular AMR (n=74) and no molecular AMR (n=223). Outcomes were measured by kidney transplant loss and eGFR decline of >30% as a combined endpoint.

Results
We followed kidney allograft biopsy cases for a median of 18 months (IQR 10,29). Molecular AMR was found in 51% of AMR cases, 62% of DSA-negative MVI cases, 13% of probable AMR cases, and 7% of cases with no AMR. After 1, 3, and 5 years after biopsy, molecular AMR cases had higher rates of the combined endpoint than no molecular AMR cases (22% vs. 6%, 40% vs. 16%, 53% vs. 25%; p<0.0001). These rates were even higher when possible molecular AMR cases with all AMR phenotype scores >0.3 (n=38) were included (59% vs. 10% at 5 years). This difference was significant in all histologic groups by Banff 2022, except for probable AMR (p=0.2). Higher mixed rejection phenotype scores (R3, p=0.003) and higher all AMR phenotype scores (p=0.044) were independent predictors of the combined endpoint among cases with molecular AMR.

Conclusion
The presence of molecular AMR is associated with higher rates of kidney allograft loss and eGFR decline in the new subgroups of AMR, DSA-negative MVI, and probable AMR. Additionally, molecular findings below the threshold may have clinical significance. Molecular rejection phenotype scores, especially the mixed rejection score and all AMR score predict outcomes independently.

PV03-11

Transcriptomic Analysis Of Kidney Allograft Biopsies May Allow Early Detection Of Rejection, Precise Rejection Typing, And Dynamic Treatment Monitoring

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Introduction

The 2022 Banff Meeting Report suggests that biopsy-based transcripts related to antibody-mediated rejection (AMR) could substitute for microvascular inflammation (MVI). In addition, transcriptomic analysis may (1) detect molecular signatures associated with rejection earlier than traditional histopathologic methods, (2) distinguish between different types of rejection more accurately, and (3) provide more quantifiable measures of treatment responses. Studies with follow-up biopsies are needed to test the performance of biopsy-based transcript analysis for these aims.

Methods

From 2018 to 2023, we examined 62 kidney transplant recipients and 139 kidney allograft biopsies evaluated by histology and the Molecular Microscope Diagnostic System (MMDx). The 62 biopsy series were analyzed regarding (1) the time of rejection diagnosis, (2) the type of rejection diagnosis, and (3) the response to treatment.

Results

Twenty, five, and eight of the initial biopsies showed histologic AMR/DSA-negative MVI, TCMR, and mixed AMR/TCMR, respectively. Molecular AMR, TCMR, and mixed AMR/TCMR were detected in 17, 4, and 8 of the initial biopsies, respectively. Follow-up biopsies were obtained at a median of 9 months (IQR 4,18) after the initial kidney allograft biopsy. With the MMDx, AMR was detected sooner in 8 cases (including probable AMR by histology), which was verified histologically by the follow-up biopsy. There were 3 cases of histologic TCMR with mixed molecular AMR/TCMR and 2 cases of histologic AMR with mixed molecular AMR/TCMR. Follow-up biopsies verified the presence of mixed AMR/TCMR in all 5 cases by histology. Using transcriptomic analyses, treatment responses were observed in 1 early active AMR and 3 mixed AMR/TCMR cases, but not by histology. Five of twenty histologic AMR cases (25%) showed no molecular AMR signature throughout the biopsy series.

Conclusion

Biopsy-based transcript diagnostics can help detect rejection sooner and identify rejection types more precisely, which might reduce the need for repeat biopsies and support treatment decisions. Molecular diagnostics may also allow clinicians to measure treatment outcomes more comprehensively through follow-up biopsies.

PV03-12

Biopsy-Based Transcript Diagnostics Show An Early Molecular AMR Signature In Cases With Probable AMR Independent From The Individual Active Histological Lesions

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Introduction

The category "suspicious for antibody mediated rejection (AMR)" in Banff 2013 was abandoned in Banff 2017, and replaced by the designations "DSA-negative microvascular inflammation" and "probable AMR" in Banff 2022. Probable AMR now represents a heterogenous group of DSA-positive cases with active AMR features (v, g, ptc, TMA) and/or chronic AMR features (cg, ptcml). Biopsy-based transcript diagnostics may add value in these cases.

Methods

We identified 64 cases with probable AMR by histology, that were categorized regarding AMR features into active (n=23), chronic-active (n=20), and chronic (n=21) cases. The Molecular Microscope Diagnostic System (MMDx) was performed in all cases, and we analyzed classifier scores and rejection phenotype scores.

Results

Among 64 cases with probable AMR, 10 cases showed molecular AMR (17%) and 6 cases (10%) showed possible molecular AMR (all AMR phenotype score >0.3). 7 of 16 cases (44%) with molecular/possible molecular AMR underwent kidney allograft biopsy for subclinical DSA. 10 of 23 cases (43%) with active AMR features, 4 of 20 cases

(20%) with chronic-active AMR features, and 2 of 21 cases (10%) with chronic AMR features showed molecular/possible molecular AMR. 6 of 14 cases (43%) with v1-lesions, 10 of 31 (32%) cases with g1-lesions, and 2 of 5 (40%) cases with ptc1-lesions showed molecular/possible molecular AMR. Among 16 cases with molecular/possible molecular AMR, median rejection phenotype scores R4, R5, and R6 were 0.29 (IQR 0.06, 0.44), 0.03 (IQR 0.00, 0.11), and 0.07 (IQR 0.01, 0.17), respectively (p=0.028). Interestingly, the 2 chronic cases with molecular/possible molecular AMR showed elevated R5 and R6 scores only.

Conclusion

Biopsy-based transcript diagnostics identify signs of molecular AMR in more than a third of cases with active AMR features by histology. These findings are independent from the individual active AMR feature v, g, and ptc. Interestingly, predominant R4 scores suggest an early molecular AMR signature. Activity and chronicity appears to be gradually reflected by rejection phenotype scores. Whether donor-derived cell-free DNA could identify those cases needs to be addressed.

PV03-14

Five-Year Kidney Function And Outcomes In Kidney Transplant Recipients Converting From Twice-Daily To Once-Daily Tacrolimus

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Introduction

CHORUS (NCT02555787) is a prospective, global, non-interventional study investigating long-term clinical outcomes in kidney transplant recipients (KTRs) who converted from twice-daily, immediate-release tacrolimus to once-daily, prolonged-release tacrolimus (PRT; Advagraf®, Astellas Pharma Europe, Ltd.) under routine practice conditions.

Methods

KTRs (≥18 years, N=4389) converting to PRT based on treating physician's judgment were enrolled. KTRs were grouped by time of conversion post-transplant to early (≤6 months, ECs) and late converters (>6 months, LCs). Primary endpoint: change in renal function (measured by estimated glomerular filtration rate, eGFR) from conversion up to 5 years. Secondary endpoints included graft and patient survival, tacrolimus dose and trough levels, donor-specific antibodies (DSA) emergence and safety.

Results

The full analysis set (FAS) included 4028 KTRs (1060 EC; 2968 LC). Most patients (60.5%) were male, with a mean age of 50.9 years and a mean eGFR of 56.05 mL/min/1.73m^2 at conversion.Overall, eGFR remained stable 5 years post-conversion, with a mean change from baseline of -1.36 mL/min/1.73m^2 (3.40 EC; -2.98 LC). There was an improvement in eGFR in ECs and a minor reduction in LCs from conversion to 12 months. At 5 years post-conversion, mean PRT dose was 3.95 mg/day (4.32 EC; 3.84 LC). At study end, 66.7% of KTRs had tacrolimus trough levels ≥5 ng/mL and >80% of KTRs had trough level coefficient of variation <35%.

5-year Kaplan-Meier estimates of patient survival was 92.9% for ECs and 98.5% for LCs; graft survival was 88.1% for ECs and 97.5% for LCs. In patients who were DSA negative prior to or at conversion 4.9% had DSA occurrence post-conversion. At study end, 70.8% of patients stayed on PRT. Adverse events (AEs) were reported in 72.4% of patients; 19.3% had ≥1 PRT-related AE. Serious AEs (SAEs) were reported in 50.6% of patients; 10.4% had ≥1 PRT-related SAE. The discontinuation rate due to AEs was 11.8% and PRT-related AEs was 5.5%.

Conclusion

Results from this large KTR cohort showed renal function remained stable overall. Patient and graft survival were high 5 years post-transplant with no unexpected safety findings, supporting PRT long-term use.

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PV03-16

Safety And Effectiveness Of Prolonged Calcineurin Inhibitor-Exposure During Belatacept Late Conversion

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Introduction
De novo belatacept-based immunosuppression protocols and late conversion from a calcineurin inhibitor (CNI)- to a belatacept-based immunosuppressive regime have been associated with a higher risk of acute rejection, especially T cell-mediated rejection (TCMR) in kidney transplant recipients (KTRs). Previous groups showed to overcome the increased risk for TCMR with a prolonged CNI-exposure in de novo protocols. In response to this, we revised our late conversion protocol to include an extended duration of concurrent CNI-administration.

Methods
From 03/2022-05/2024, 39 KTRs, transplanted at least 12 months prior, were converted to belatacept with a concurrent CNI-exposure of 3 months (n=5) or 6 months (n=34) post-conversion, based on individual immunological risk assessments. CNIs were tapered to low trough levels (2-4 µg/l) after 1 month. CMV-, EBV- and BKV-replication were routinely screened at month 3, 6 and 12 after conversion, with other infections documented as they occurred. Anti-HLA donor-specific antibodies (DSA) were screened at baseline and after 12 months, or at the time of an indication biopsy. All patients were followed for 12 months after conversion, with documentation of infections, de novo DSA (dnDSA) and biopsy-proven acute rejections (BPAR).

Results
5/39 (12.8%) patients had infections associated to conversion, needing medical treatment, including 1 case of CMV-associated diarrhea, 3 cases of bacterial pneumonia and 1 case of cellulitis. There were no other relevant CMV-, BKV-, or EBV-replications, and no fungal infections. At 1 year post-conversion 7/39 (17.9%) patients showed development of dnDSA, 2 against HLA-Class I dnDSA, and 5 against HLA-Class II dnDSA, with a mean fluorescence intensity (MFI) between 500-1000 (median 602, interquartile range 527-610). No BPAR was objectified in the first year post-conversion.

Conclusion
Our revised belatacept conversion protocol demonstrated a moderate rate of associated infections, comparable to previous studies. No dnDSA with an MFI >1000 and no BPAR (especially TCMR) were observed. Further investigation is needed to assess the long-term outcomes of this new conversion protocol.

Poster Session 04: Kidney in General / Pancreas

PV04-01

Pancreas Transplantation As Rescue Therapy In A Patient With Type 1 Diabetes And Concurrent Subcutaneous Insulin Resistance

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Introduction
Patients with type 1 diabetes and concurrent subcutaneous insulin resistance present unique diagnostic and therapeutic challenges for clinicians. The standard therapeutic approach is the administration of intravenous insulin. Pancreatic transplantation should be considered at an appropriate time, particularly in the event of life-threatening hyperglycemia, hypoglycemia, catheter-associated thromboses and infections.

Methods
We present the case of a 24-year-old female patient with type 1 diabetes since early childhood and increasingly uncontrollable subcutaneous and intramuscular insulin resistance. Furthermore, we present the diagnostic pathway and therapeutic interventions performed, culminating in pancreatic transplantation as a curative approach.

Results
Immediate graft function resulted in optimal glycemic control.

Conclusion
We propose pankreastransplantation as a possible long-term curative approach for type 1 diabetes and concurrent subcutaneous insulin resistance. Pankreastransplantation provided glycemic control and improved quality of life in our patient.

PV04-02

The Routine Use Of Magnetic Double-J Stents in Kidney Transplantation – A Single-Center Retrospective Study

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Introduction
The insertion of a ureteral stent after ureteroneocystostomy is considered the gold standard for reducing postoperative ureteral complications in kidney transplantation. Previously, this necessitated cystoscopic removal, which is often described as painful and is therefore associated with fear. To our knowledge, there are only two publications on the use of magnetic DJ stents in kidney transplantation [1,3]. Following a successful case series and a randomized study involving a total of 30 transplants, both conducted in our Transplant Center, magnetic DJ stenting is now routinely used in our center [4]. Numerous studies have already demonstrated the removal of magnetic DJ stents to be significantly less painful [2,5]. Therefore, this study aims to evaluate the magnetic DJ stent concerning postoperative ureteral complications in kidney transplantation.

Methods
This retrospective study includes all magnetic DJ stents used in our Freiburg Transplant Center from January 2020 to May 2024. We exclusively used the Magnetic Black Star® from Urotech GmbH (Medi-Globe Group, 83101 Rohrdorf, Germany). Application was irrespective of living or postmortal kidney donation, ABO compatibility, and was also applied in autotransplantations, kidney-pancreas transplantations and pediatric cases. The removal was routinely performed on our general ward

or outpatient clinic if the patients had already been discharged. Antibiotic prophylaxis with amoxicillin/clavulanic acid was administered 2 days prior to removal.

Results

A total of 346 kidney transplantations were performed during the study period; of which 318 were ABO-compatible, 28 were ABO-incompatible, 4 were autotransplantations, and 7 were kidney-pancreas transplantations. In 303 cases, the magnetic DJ stent was implanted, including 22 pediatric patients. The removal using a retrieval device was successful in 96,4% of cases. Compared to the previously used conventional ureteral catheters, urinary tract infection rate did not increase. Additionally, postoperative ureteral complications, such as stenosis or leakage, were comparable to the previous years.

Conclusion

In our center, the use of magnetic DJ catheters in kidney transplantation was found to be safe and effective.

References

[1] Capocasale E, Cremaschi E, Valle RD, Ferretti S, Pellegrino C, Iaria M, Puliatti C (2019) Implementing a Ureteric Magnetic Stent in the Kidney Transplant Setting: Report of 100 Consecutive Cases. Transplantation 103:2654

[2] Cheng C, Ma Y, Jin S, Wen J, Jin X (2023) Comparison of the Removal Efficiency and Safety of Magnetic Versus Conventional Ureteral Stents: A Systematic Review and Meta-analysis. Eur Urol Open Sci 52:22–29

[3] Kapoor A, Akerman J, Wong ECL, Vasisth G, Hassan F, Tajzler C, Piercey K, Hoogenes J, Lambe S (2021) Comparison of a magnetic retrieval device vs. flexible cystoscopy for removal of ureteral stents in renal transplant patients: A randomized controlled trial. Can Urol Assoc J 15:E97–E102

[4] Pohlmann PF, Kunzelmann M, Wilhelm K, Miernik A, Gratzke C, Jud A, Pisarski P, Jänigen B (2019) Magnetic Ureteral Stents Are Feasible in Kidney Transplant Recipients: A Single-Center Experience. Int J Organ Transplant Med 10:162–166

[5] Rassweiler M-C, Michel M-S, Ritter M, Honeck P (2017) Magnetic Ureteral Stent Removal Without Cystoscopy: A Randomized Controlled Trial. Journal of Endourology 31:762–766

PV04-03

Kidney Transplant Plus/Minus An Angiomyolipoma

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Introduction

Thus far, there are few case reports which outline the course of transplanting a kidney with benign malformations like cysts or angiomyolipomas which have either been surgically removed 'backtable' before transplantation or have been transplanted originally as they are. In this case report, we want to outline another successful case of kidney transplantation plus/ minus an angiomyolipoma.

Methods

In May 2024, a 54 year-old mother donated her right kidney with a CT graphic tumor to her 30 year-old daughter who had been dependent on dialysis due to chronic kidney insufficiency for one year. In a preoperative CT scan in February 2024, the tumor of the mother's right kidney was most likely classified as an angiomyolipoma due to its morphology with an diameter of 6.2cm and involvement of the pelvis of the kidney. After having surgically removed the mother's kidney in a minimally invasive manner called HARP (hand assisted retroperitoneoscopic nephrectomy), the angiomyolipoma was removed 'backtable' and its' dignity was confirmed by fresh frozen section. Afterwards, the kidney's pelvic system was reconstructed by a team of transplant surgeons and urologists and finally, the reconstructed kidney could be regularly transplanted to the daughter's right pelvic.

Results

In the short-term postoperative course, we can report stable graft function and good urine excretion of the transplanted kidney.

Conclusion

This clinical case shows the potential of benignly abnormal kidneys for transplantation. Firstly, kidneys which

meet the criteria for surgical removal in order to assure the dignity of abnormal features, could be used for transplantation. Secondly, willing kidney donors would not have to be excluded due to abnormal features of their kidney. In the end, the pool of possible organ donors could be widened, more organs could be transplanted and more people with end-stage kidney failure could be helped.

PV04-04

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 over 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, mixed logistic regression analysis is used.

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.

References

[1] Frei U, Noeldeke J, Machold-Fabrizii V et al: Prospective age-matching in elderly kidney transplant recipients – a 5-year analysis of the Eurotransplant Senior Program. Am J Transplant, 2008; 8: 50–57

[2] Oniscu GC, Brown H, Forsythe JL. Impact of cadaveric renal transplantation on survival in patients listed for transplantation. J Am Soc Nephrol 2005; 16: 1859–1865

[3] Lee CM, Carter JT, Randall HB et al: The effect of age and prolonged cold ischemia times on the national allocation of cadaveric renal allografts. J Surg Res, 2000; 91: 83–88

[4] Kruger B, Zulke C, Fischereder M et al: Early experience with the ET Senior Program "Old For Old"; better to be number one? Transpl Int, 2002; 15: 541–45

PV04-05

Fit For Kidney Transplantation Through Rehabilitation

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Introduction

The decline in physical performance and the associated increase in the risk of frailty particularly jeopardize the transplantability status in the long term among older patients on the waiting list for a kidney transplant. The project "Fit für die Nierentransplantation durch Rehabilitation" aims to reduce this risk and optimize preparation for potential transplantation through an interdisciplinary care program [1,2].

Methods

In this intervention study, 91 patients are longitudinally analyzed (aged >65, on the waiting or pre-waiting list for transplantation). In addition to a possible three-week inpatient rehabilitation, patients receive individualized sports and nutritional science support as a supplement to standard care [3,4]. To evaluate the effectiveness of the project, patients undergo biannual assessments of physical performance, body composition, quality of life, and bone density. Data analysis is carried out descriptively using mean comparisons over the long term.

Results

The current comparison of data at baseline and after one year (n=51) demonstrates significant improvements in Berg Balance Scale (BBS) (+1.0 points ± 3.0; p=0.009), waist circumference (-3.6 cm ± 5.1; p<0.001), BMI (-0.8 kg/m^2 ± 1.5; p<0.001), Frailty Scale (-0.4 points ± 1.0; p=0.003), and Barthel Index (+3 points ± 8.8; p=0.035). Even after two years (n=20), the positive effects on BBS (+3 points ± 7.5; p=0.003), waist circumference (-4.1 cm ± 7.7; p=0.015), BMI (-0.9 kg/m^2 ± 2.0; p=0.034), and Barthel Index (+3 points ± 7.5; p=0.045) remain significant. Further tests of physical performance show no significant changes. Blood values also show no significant changes.

Conclusion

The need for interdisciplinary care of patients on the waiting list for a kidney transplant underscores the necessity for sustainable strategies to enhance and maintain physical resources to ensure long-term transplant eligibility throughout the waiting period [5]. By integrating this additional care service, the project can make a significant contribution to the lasting improvement of physical performance in this patient group.

References

[1] Wilkinson, TJ, Shur, NF, Smith, AC 2016, 'Exercise as medicine" in chronic kidney disease', *Scandinavian Journal of Medicine & Science in Sports*, 26(8), 985-8

[2] Goldberg, AP, Geltman, EM, Gavin, JR, Carney, RM, Hagberg, JM, Delmez, JA, Naumovich, A, Oldfield. MH, Harter, HR 1986, 'Exercise training reduces coronary risk and effectively rehabilitates hemodialysis patients', *Nephron*, 42(4), 311-6.

[3] Sheshadri, A, Johansen, KL 2017, 'Prehabilitation for the Frail Patient Approaching ESRD', *Seminars in nephrology*, 37(2), 159-72.

[4] Kouidi, E 2002, 'Exercise training in dialysis patients: why, when, and how?', *Artifical Organs*, 26(12), 1009-13

[5] Clarkson, MJ, Bennett, PN, Fraser, SF, Warmington, SA 2019, 'Exercise interventions for improving objective physical function in patients with end-stage kidney disease on dialysis: a systematic review and meta-analysis', *American Journal of Physiology-Renal Physiology*, 316(5), 856-72

PV04-06

Smart & Fit For Kidney Transplantation

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Introduction

The decline in physical performance and the associated increase in the risk of frailty jeopardize the transplantability status in the long term for all age groups on the waiting list for kidney transplantation. The study "Smart & Fit für die Nierentransplantation" investigates the effects of

additional interdisciplinary care on body composition and physical performance before kidney transplantation [1,2,3].

Methods

This is a randomized controlled intervention study, in which approximately 150 patients (aged >65, on the waiting or pre-waiting list for transplantation) are to be included. Body composition (BMI, waist circumference, muscle and fat composition), physical performance (mobility, strength, endurance, and balance), quality of life, blood parameters (potassium, phosphate, HbA1c, etc.), level of independence, and fatigue will be examined over one year. The control group will receive an information app for self-study in addition to standard care. The intervention group will receive individualized nutrition and exercise counseling in addition to the app, as well as a 3-week inpatient rehabilitation. Patients are reevaluated at six months and again at one year post-initial assessment Data analysis will initially be descriptive based on mean comparisons.

Results

At present, no meaningful results can be presented over time. However, by the time of the annual meeting of the German Transplantation Society, sufficient data will be available for analysis of results after six months, allowing for the presentation of initial findings. In the baseline examinations (currently n=119), a high proportion of patients were found to suffer from fatigue and physical inactivity.

Conclusion

The need for additional services for patients on the waiting list for kidney transplantation is particularly high due to the risk of frailty or low physical performance [4]. Therefore, new forms of care are necessary to maintain the possibility of transplantation in the long term. Additionally, assessing physical performance may help identify risk factors, thereby facilitating the implementation of preventative measures [5].

References

[1] Wilkinson, TJ, Shur, NF, Smith, AC 2016, 'Exercise as medicine" in chronic kidney disease', *Scandinavian Journal of Medicine & Science in Sports*, 26(8), 985-8

[2] Sheshadri, A, Johansen, KL 2017, 'Prehabilitation for the Frail Patient Approaching ESRD', *Seminars in nephrology*, 37(2), 159-72.

[3] Deligiannis A, Kouidi E, Tassoulas E et al. 1999, 'Cardiac effects of exercise rehabilitation in hemodialysis patients.' *Int J Cardiol* 70:253-266

[4] Johansen KL, Chertow GM, Jin C et al. 2007, 'Significance of frailty among dialysis patients.' *J Am Soc Nephrol* 18:2960-2967

[5] Mcadams-Demarco MA, Ying H, Van Pilsum Rasmussen S et al. 2019, 'Prehabilitation prior to kidney transplantation: Results from a pilot study.' *Clin Transplant* 33:e13450

PV04-07

Prognostic Significance Of Zero Biopsies After Reperfusion For Organ Survival After Kidney Transplantation

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Introduction

Nullbiopsien nach Reperfusion im Rahmen der Nierentransplantation bieten Informationen zur Bewertung der Transplantatqualität. Der prädiktive Wert der Histologien ist allerdings noch nicht hinreichend geklärt.

Methods

338 Transplantatbiopsien mit Entnahme 10 Minuten nach Reperfusion wurden retrospektiv eingeschlossen. 243 Proben stammen von Postmortalspenden und 95 von Lebendspenden. Die Nullbiopsien wurden nephropathologisch gemäß BANFF anhand der Ausprägung der histologischen Merkmale, Glomerulosklerose (GS), interstitielle Fibrose und tubuläre Atrophie (IFTA), Arteriosklerose (AS) und akute Tubulusschädigung (ATI, engl. acute tubular injury) beurteilt. Assoziationen wurden mittels

multivariater Cox-Regression und binären Regressionsanalysen untersucht.

Results

Die maximale Nachbeobachtungszeit betrug 11,4 Jahre, wobei es bei 108 Fällen (32%) zu einer verzögerten Transplantatfunktion (DGF, engl. delayed graft function) kam. ATI und AS waren signifikant mit DGF assoziiert (ATI > 50%: OR 2,28, 95% CI 1,26 - 4,13; AS > Grad 1: OR 2,48, 95% CI 1,44 - 4,27). Die univariate Cox-Regression zeigte Assoziationen von IFTA und GS mit dem todeszensierten 1-Jahres-Transplantatüberleben (IFTA: HR 1,82, 95% CI 1,18 - 2,80, p = 0,007; GS: HR 1,27, 95% CI 1,01 - 1,61, p = 0,036) und über den ganzen Beobachtungszeitraum (IFTA: HR 1,70, 95% CI 1,24 - 2,33, p = 0,001; GS: HR 1,19, 95% CI 1,01 - 1,39, p = 0,033). Multivariate Cox-Regressionsanalysen, die bekannte klinische Risikofaktoren wie den Expanded Criteria Donor-Status, Diabetes des Spenders und HLA-Mismatches berücksichtigen, zeigten keine mit histologischen Markern bestehende Assoziationen mit dem todeszensierten 1-Jahres-Transplantatüberleben. Nur IFTA zum Zeitpunkt der Transplantation und HLA-Mismatches waren auch nach multivariater Analyse prädiktiv für das todeszensierte Transplantatüberleben.

Conclusion

Unsere Untersuchungen charakterisieren die prognostische Wertigkeit von post reperfusionem entnommenen Nullbiopsien. Dabei erwies sich einzig das Ausmaß der IFTA als prädiktiv für das Transplantatüberleben. Sie liefern damit einen Beitrag zur Einordung der Qualität von Spendernieren anhand histologischer Charakteristika.

Reference

[1] Nachname, V, Nachname, V JJJJ, 'Artikel', *Journal*, Ausgabe, Seite, Erscheinungsort: Herausgeber Wang, C.J., Wetmore, J. B., Crary, G. S., Kasiske, B. L., 'The Donor Kidney Biopsy and Its Implications in Predicting Graft Outcomes: A Systematic Review', *American Journal of Transplantation*, 15, 1903–1914, Durham, NC: Wiley Periodicals Inc.

PV04-08

Easy And Reliable Discrimination Between Temporary And Persistent Renal Graft Dysfunction By Novel Acetate Turnover Test Prior To Transplantation

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Introduction

Despite shortage of donor organs, a lot of grafts are discarded due to questionable quality. Normothermic machine perfusion offers a platform for pre-implantation evaluation of the graft, but many kidneys are afflicted by transient filtration failure early after preservation. Therefore, classical renal function tests are not applicable to differentiate between prospective recovery or continuing deficit of renal function. Here, we develop and test a non-invasive quantitative method that can measure the biochemical reaction that correlates to the viability of isolated kidneys using pig kidneys as a model system.

Methods

We present an evaluative approach based on metabolic turnover of ^{13}C-acetate during isolated perfusion. After injection of the tracer, its turnover by the citrate cycle can be quantified by direct detection of $^{13}CO_2$ in the gas outflow of the oxygenator with a mobile, high precision laser spectrometer. Porcine kidneys were subjected to varying degrees of ischemic injury prior to retrieval (0; 30; 60min), matched to established graft outcome data after renal transplantation (1:healthy, 2:regaining function 1-2days after transplantation, and 3: persistent non-function).

Results
While many parameters (e.g. clearance, urine flow, biomarkers) could discern good grafts from the others, only the rate of ^{13}C-acetate metabolization turned out to separate group 2 from group 3, even with rather high accuracy (area under the ROC curve 0.91; P<0.001). This would be of clinical importance in so far as the former might successfully be transplanted, while the challenge lies in the recognition and discard of those grafts, that are not likely to recover after engraftment.

Conclusion
Thus, the ^{13}C turnover test appears to have the potential of an objective, quantitative and valuable adjunct in the toolbox for pre-transplant evaluation of questionable renal grafts.

PV04-09

A Comorbidity And Age Based Stratification Improves Graft And Overall Survival In Kidney Transplantation

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Introduction
We herein aimed to develop an easy-to-use tool that stratifies waiting list candidates for kidney transplantation into risk groups, similar to the Charlson Comorbidity, to improve waiting list management.

Methods
We enrolled 474 adult patients who underwent kidney transplantation at two German centers between 2018 and 2023. Based on their comorbidities and age at time of listing, patients were divided into three different morbidity severity groups: I (end-stage renal disease with typical comorbidities such as arterial hypertension or diabetes mellitus), II (one additional diseased vital organ system), III (two additional diseased vital organ systems or age over 65 years). Data for each recipient were retrospectively analyzed for mortality or graft loss, estimated glomerular filtration rate (eGFR using the CKD-EPI formula), and albumin-to-creatinine ratio (ACR) one year after transplantation.

Results
With regard to mortality, the results showed a trend toward differentiation between the three clinical grading groups 1 year after transplantation (p = 0.022, HR 3.85 [I vs. II], HR 6.55 [I vs. III]). However, there was a clear difference when graft loss was included in the analysis or mortality was censored for graft loss (p = 0.037 and p = 0.012, respectively). Clinical grades and eGFR at one year post-transplant correlated well (all p < 0.05) with group I showing 55.8 mL/min/1.73m^2, group II showing 47 mL/min/1.73m^2 and group III showing 39.1 mL/min/1.73m^2. When patients from the European Senior Program and the Acceptable Mismatch Program were excluded, these differences persisted. Notable differences in ACR were observed only between groups II and III (p = 0.004).

Conclusion
Stratification of waiting list patients into three grading groups based on age and comorbidities can predict patient outcomes one year after kidney transplantation with respect to mortality, graft loss, and graft function. The use of this simple categorization tool may improve the management of the waiting list e.g., by defining different intervals for re-evaluation and using this information in organ allocation strategies.

PV04-10

Kidney Transplantation From Octogenerian Donors – A Single Center Experience

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Introduction
In times of organ shortage, multiple strategies to enlarge the donor pool have to be developed. Introduction of the Eurotransplant senior program brought the opportunity to use kidneys from older donors for older recipients. Kidneys from very old donors aged 80 years or older enlarge the risk for organ failure or reduced long term results but may offer another option to enlarge the number of patients treated with kidney transplantation.

Methods
All kidney transplantations with usage of organs from octogenarian donors at Hanover medical school between January 2006 and September 2023 were included in this study. Patient and graft survival was well as PNF, DGF and creatinine clearance during follow up were taken from patients records.

Results
71 kidney transplantation from octogenarian donors were included. 7 % suffered from PNF, 12.7 % had a DGF. 18.3 % were treated due to rejection. 5 year patient survival was 68.8 %, 5 year graft survival 65.3 % respectively. CIT had no significant influence on graft function, occurrence DGF had no influence on graft survival.

Conclusion
Good selected grafts from octogenarian donors are a justifiable option to enlarge donor pool for kidney transplantation in times of organ shortage, especially for old recipients who are under high risk for complications due to dialysis.

PV04-11

IgA-Nephropathy: Results After Kidney Transplantation 2018-2023

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Introduction
IgA-nephropathy has an incidence of 2–10 per 100,000 person/years, accounting for 25% of diagnosed kidney diseases upon biopsy in Europe. Pogression of the disease leads to kidney failure, dialysis and kidney transplantation, even though many cases remain undiagnosed. Some patients are viable for a living donor transplant, preemptively before dialysis. An important issue when performing a kidney transplant for this disease is the recurrence of IgA-nephropathy in the transplanted organ [1,2]. Here, we present our results within this group of patients between 2018 - 2023.

Methods
We evaluated patients transplanted at our center for IgA-nephropathy between 2018 - 2023 analyzing patient-related data: mismatch, ischemia time, immunosuppressive induction treatment, postoperative complications, rejection, graft function and recurrence of the disease in the transplanted organ.

Results
The analyzed group contained a total of 26 patients. 12 of the procedures were performed as living donor transplantations. The mean age was 52,76 $\pm$ 14,66 years. Most patients had dialysis prior to transplant for a mean time of 3 years, in 4 cases procedures were performed as preemptive transplants. The mean warm ischemia time was around 48,6 $\pm$ 21,56 minutes, with a cold ischemia time of around 476,52 $\pm$ 285,21 minutes. We experienced several cases of rejection post transplantation (Borderline/BANF 1 A), especially among the group induced preoperatively with basiliximab (1 % vs 37,5 %). Two organs had to be explanted because of venous thrombosis (n=2, 7,6 %). Two cases experienced recurrence of IgA-nephropathy upon biopsy of the transplanted organ (n=2, 7,6 %). All cases have been biopsied during follow-up, however there were no routine biopsies immediately postop. One preemptive case had to be put on intermittent dialysis because of insufficient graft function (n=1, 3,8 %). Graft function after a follow-up period of 51 $\pm$ 18 months remained in most cases stable, with mean serum creatinine levels of 1,96 $\pm$ 0,57 mg/dl.

Conclusion
IgA-nephropathy is a systemic disease, which can lead to graft failure after kidney transplantation. In our experience, the recurrence rate is low with overall good short and midterm results.

References

[1] Rajasekaran A, Julian BA, Rizk DV. IgA Nephropathy: An Interesting Autoimmune Kidney Disease. Am J Med Sci. 2021 Feb;361(2):176-194. doi: 10.1016/j.amjms.2020.10.003. Epub 2020 Oct 8. PMID: 33309134; PMCID: PMC8577278.

[2] Rodrigues JC, Haas M, Reich HN. IgA Nephropathy. Clin J Am Soc Nephrol. 2017 Apr 3;12(4):677-686. doi: 10.2215/CJN.07420716. Epub 2017 Feb 3. PMID: 28159829; PMCID: PMC5383386.

PV04-14

Radical Prostatectomy In Kidney Transplant Recipients – A Multicenter Experience At Nine German Urologic Transplant Centers

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on behalf of the German Society of Residents in Urology (GeSRU) Academics Kidney Transplantation Work Group

Introduction

Kidney transplant recipients (KTRs) face a heightened risk of genitourinary cancers. Among these, prostate cancer (PCa) is expected to rise with the aging KTR population. Understanding the surgical outcomes of curative intended surgery for PCa in this unique group is crucial.

Methods

Data from 62 KTRs who underwent radical prostatectomy (RP) between 2006 and 2023 across nine urologic transplant centers were analyzed. Complications were graded with the Clavien-Dindo classification. Perioperative results were assessed, and oncologic follow-up was conducted. Overall survival (OS), biochemical recurrence-free survival (BRFS), and death-censored graft survival were calculated using the Kaplan-Meier method and log-rank testing.

Results

We included 50 open radical retropubic (ORRP) and 12 robot-assisted radical prostatectomies (RARP). RARP showed lower blood loss but longer operative time. Half of the patients experienced no postoperative complications, while 14.5% experienced grade 3 or higher complications. These complications included drainage of a lymphocele in 3 cases, wound revision in 3 cases, and surgical revision for postoperative bleeding in 2 cases. No graft losses were linked to RP. Pathological examination showed pN1 in 8.1% and positive surgical margins in 25.8% overall - but particularly only 8.3% of the pT2 tumors. Median follow-up was 48.5 months, showing median OS of 128 months (95%CI 71.2-184.8), BRFS of 106 months (95%CI 55.8; 156.2), and graft survival of 127 months (95%CI 66.7-187.3). Retrospective design and variations among groups and centers were limiting factors of interpretation.

Conclusion

The results show that radical prostatectomy (RP) is a safe treatment for localized prostate cancer in kidney transplant recipients, with satisfactory cancer treatment outcomes. This procedure, performed by specialized urologists on carefully selected patients with curative intent, has minimal effect on the transplanted kidney's function. It is essential to be vigilant in screening and identifying the risk of understaging the cancer stage.

PV04-15

Administration Of Non-Vitamin K Antagonist Oral Anticoagulants In Renal Transplant Recipients With Atrial Fibrillation: A Single-Center Experience

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Introduction
Atrial fibrillation (AF) is associated with increased stroke risk in patients with chronic kidney disease (CKD) including renal transplant recipients (RTRs). Little is known about the real-life dose administration of non-vitamin K antagonist oral anticoagulants (NOACs) in RTRs in terms of graft function.

The study aimed to analyze the adjustment of NOACs dose in the study population in terms of kidney graft function.

Methods
In this retrospective cohort study, we enrolled 163 (M-65,6%) RTRs with AF in median age 66 years, mean level of creatinine 1,62mg/dl, and creatinine clearance (CC) (Cockroft-Gault equation) 47,9ml/min, including 139 (82.7%) subjects on apixaban (daily dose) 5mg (n-84) or 10mg (n-55), 18 (10.7%) on rivaroxaban (daily dose) 15mg (n-14) or 20 mg (n-4), 6 (3.6%) on edoxaban 30 mg/day.

Results
In the group with apixaban treatment 110 RTRs, had CC ≥30ml/min. 49,1% of them used the standard dose of 10mg and 50,9% used the too-low dose of 5mg. 26 RTRs had CC 15-29ml/min (96% used the standard dose of 5mg according to low CC, appropriately) and 3 with CC <15ml/min were treated with 5mg, inappropriately.

5 RTRs under rivaroxaban treatment had CC ≥50ml/min. 60% of them used the standard dose of 20mg and 40% used the too-low dose of 15mg /day. 13 RTRs had CC 15-49ml/min (92,3% used the dose of 15mg according to low CC, appropriately).

Edoxaban 30mg/day (too-low dose) was used in 1 RTRs, who had CC ≥50ml/min. 5 RTRs with CC 15-49ml/min (100% used the standard dose of 30mg according to low CC).

Conclusion
In most RTRs, NOACs doses were not adequate for kidney graft function.

Underdosing drugs in RTRs population may contribute to a higher rate of stroke and death with a functioning graft.

Poster Session 05: Basic Science

PV05-01

Ex vivo Immunologic Conditioning – A Novel Role For Type 1 Interferons?

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Introduction
Type 1 Interferons (T1IFN) are mediators of the immune system and have been associated with injury in warm ischemia of the kidney. However, data on their role in cold ischemia (CI) is scarce. Unpublished results of our group showed an elevated release of T1IFN in rat kid-

ney transplants with a longer CI period. Aim of our study was to explore the role of T1FN in CI with the purpose of immunologic conditioning.

Methods
Kidneys of Fischer rats were perfused at 4°C with UW-CS and harvested. The left kidneys underwent, after a median of 145 min CI, normothermic *ex vivo* machine perfusion with Krebs-Henseleit buffer (KHB). The right kidneys were stored at 4°C as controls. In some experiments, inhibitors of the cGAS/STING system or other immunosuppressive agents were added to KHB for perfusion. Porcine aortic endothelial cells (PAEC) were exposed to 4°C in UW-CS, HTK, HTK with deferoxamine (HTKD, 1 mM), Custodiol-N (CN) or Custodiol-MP (CMP) for 4 or 16 hours followed by rewarming to 37°C in KHB for 3 hours. Expression of T1IFN from kidney- or cell lysates was studied via RT-PCR.

Results
Ex vivo normothermic perfusion of the kidneys increased the expression of IFN-β 250-fold. Inhibition of the cGAS/STING pathway reduced this effect. Application of chloroquine had a similar impact. Expression of IFN-α showed a 10-fold increase compared with the controls. Inhibition of cGAS/STING or utilization of other immunosuppressive agents failed to influence this effect. Expression of IFN-β rose markedly in PAEC after rewarming in case of 16 hours of cold storage in UW-CS, HTK or HTKD. A 4-hour cold storage or the application of CN or CMP prevented this effect. However, expression of IFN-α showed a significant decrease independently of solution or duration of cold storage.

Conclusion
Simulated reperfusion after CI of rat kidneys increases the expression of IFN-β which is mediated by the cGAS/STING system and could implement a role for free dsDNA in the cytosol. On the other hand, PAEC showed a similar increase in IFN-β expression upon rewarming, although IFN-α showed a different pattern. In conclusion, endothelial cells are a potential source of the increased IFN-β production.

PV05-02

Core Signature Of Rejection-Specific Cytokines And Chemokines In Heart Biopsies After Transplantation

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Introduction
Allograft rejection remains one of the limiting factors for survival after HTX. The aim of this project was to characterize the cytokine/chemokine network in heart biopsies and peripheral blood plasma after HTx. The quantified cytokine/chemokine concentrations could reflect the ischemia/reperfusion response as well as rejection status of the allograft. Therefore, we hypothesize that in heart biopsies with histopathological proven acute rejection the microenvironment is significantly altered and potentially specific cytokine/chemokine patterns could predict allograft rejection.

Methods
Heart biopsies (N=181 biopsies; 52 patients) and peripheral blood samples (N=147 samples; N=52 patients) were obtained between 6d and 5yrsafter HTX. Using Luminex-based multiplex assays 50 immune mediators in tissue lysates and peripheral blood plasma were quantified. Concentrations of samples with histopathologic confirmed acute rejection and without signs of acute rejection were compared in lysates and plasma. Moreover correlation of tissue and plasma was performed.

Results
With regard to the rejection status we identified significant differences in lysate concentrations. Especially CXCL9/MIG, CXCL4/MIP-1β and CXCL10/IP-10 showed significantly elevated concentrations in biopsies with proven rejection ($p<0.001$). In addition, we identified individual long-term changes of single patients after transplantation and significant differences comparing tissue lysates with plasma concentrations. Interestingly, we found no strong correlation between plasma and lysate concentrations.

Conclusion
We could detect a core signature for biopsies with pathologically secured acute rejection consisting of increased concentrations of the chemokines CXCL9/MIG, CXCL10/IP-10, CXCL3/ MIP-1α and CXCL4/MIP-1β. This signature is clearly distinguished from the pattern we found in matched plasma samples and importantly there was no correlation between the measured protein concentrations in plasma and tissue lysates. Therefore, we hypothesize that biopsies remain indispensable for the diagnosis of heart rejection.

PV05-03

Establishing Porcine Wild-Type Hepatocyte Spheroid Formation As An *In Vitro* Long-Term Liver Perfusion Model: Preliminary Findings And Potential For Translational Research

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Introduction
Liver transplantation is crucial for end-stage liver disease. Extracorporeal machine perfusion, particularly with marginal organs or in an experimental setting, is a promising approach to address organ shortage. Long-term perfusion aids organ treatment before transplantation. Yet, perfecting long-term protocols is ongoing, necessitating *in vitro* studies on perfusion solutions' impact on hepatocyte function. Hepatocyte spheroid models provide a platform for optimizing perfusion models. We present initial findings on establishing a porcine wild-type hepatocyte spheroid for *in vitro* perfusion studies and advancing transplantation research.

Methods
This study compares spheroid formation, morphology, and function of wild-type hepatocytes from porcine donors under various preservation conditions. A standardized protocol was established for evaluating spheroids in a modified William E medium (+ 20% FCS; + 0.01 U/ml Insulin, + 1 U/ml heparin), autologous porcine blood, and HKT solution, maintained at 37°C with 5% CO2, in an oscillation bioreactor. Spheroids were cultured for 6 days, and cell viability was assessed every 24 hours using the alamarBlue assay.

Results
Following collagenase-based hepatocyte isolation, wild-type porcine hepatocytes exhibited satisfactory quantity (205 ± 83 million hepatocytes) and vitality ($75\%\pm8\%$) prior to spheroid formation. The alamarBlue assay demonstrated sustained viability over 6 days, notably higher in cultures with autologous porcine blood (82.2% viability at 1:2 dilution, 63.4% at 1:4 dilution) compared to standard medium. Spheroids preserved in HKT solution at 37°C exhibited an 88% decrease in viability (82.8% decrease with HTK at 4°C).

Conclusion
These preliminary results present a promising *in vitro* testing platform, particularly when considering its potential use in evaluating preservation conditions for specific cell types within an experimental pre-organ context. Further optimization is essential to enhance this model's applicability in liver regeneration research, enabling translational cell therapy investigations.

PV05-04

Pirfenidone And Nintedanib Individually Reduce Chronic Rejection In A Murine Aortic Transplant Model But Not In Combination

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Introduction
Almost 50% of heart transplant recipients develop cardiac allograft vasculopathy after transplantation, yet it remains without treatment. Affected coronary vessels show leukocyte immigration and smooth muscle cell proliferation - resulting in neointima development and graft ischemia. Albeit both are antifibrotics, pirfenidone and nintedanib differ in their underlying pathways.This study evaluates whether single or combined treatment with pirfenidone and nintedanib decreases chronic rejection in a murine transplantation model.

Methods
Allogeneic thoracic aortas from C57BL/6 mice ($H2^b$) were transplanted into the abdominal aortas of CBA mice ($H2^k$) (n= 9 / group). All mice were aged between 8 and 12 weeks and equal parts female and male. After transplantation, mice were divided into a control group and 3 treatment groups: 0.5% pirfenidone diet (PFD), 60 mg/kg oral nintedanib daily (Ninte) or both (P+N). Aortic grafts were harvested on day 14 for gene expression analysis and day 30 for (immuno-)histological analysis.

Results
Both PFD- and Ninte-treated grafts showed significantly reduced neointima formation compared to control (PFD 32.7% ± 16.7, Ninte 33.3% ± 18.5 vs. 44.0% ± 19.2, $p<0.05$). Interestingly, combined treatment did not diminish luminal occlusion (43.3% ± 21.7 vs. 44.0% ± 19.2). All treatments were able to reduce intimal smooth muscle actin with PFD being the most effective (PFD 7.0% ± 6.4, Ninte 9.1% ± 6.7, P+N 7.2% ± 8.1 vs. 12.1% ± 8.0, all $p<0.05$). While CD4+ T cells were not affected by any treatment, PFD and Ninte could significantly decrease CD8+ T cell and dendritic cell (DC) infiltration (CD8: PFD 1.8% ± 1.1, Ninte 1.5% ± 1.1 vs. 2.2% ± 1.5, $p<0.05$; DCs: PFD 4.0% ± 3.8, Ninte 2.5% ± 2.5 vs. 5.8% ± 6.4, $p<0.05$). In addition, PFD markedly reduced intragraft gene expression of proinflammatory cytokines, selectins and adhesion molecules, whereas they were largely unaffected by Ninte and slightly less so by the combined treatment.

Conclusion
The results indicate that PFD and Ninte application reduce chronic rejection in an aortic transplantation model. However, the combined treatment did not provide the expected additional benefit, but may negatively influence each other.

PV05-05

Metabolite-Enhanced Normothermic Machine Perfusion Improves Kidney Transplant Viability

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Introduction
NMP is a method of organ preservation designed to increase the success rate of transplantable organs. It has demonstrated notable benefits during liver and lung transplantation, and has even shown potential to restore brain function hours after death. For kidney, no such success has been reported so far.

Methods
We describe a novel systems biology-based framework to enhance kidney normothermic machine perfusion (NMP).

Results
To understand and overcome the factors hindering the effectiveness of kidney NMP, we took a three-step approach. First, we performed multimodal profiling of mouse tissues after NMP using a literature-based consensus buffer, including metabolomic, transcriptomic and targeted spatial proteomics. This was complemented by histopathological and ultrastructural characterization of cell injury. Together, we generated the first cell injury atlas associated with NMP, which was validated across different species, including mouse, rat, pig and human. Second, this resource was leveraged to re-engineer the most critical building block of perfusion systems, the perfusion solution, using 7 key citric acid cycle metabolites. This led to the generation of a new perfusion buffer, which we call metabolite-enhanced perfusion solution (MEPS). Third, we then tested MEPS in NMP models in mice, rats, pigs, and humans. We carefully demonstrate an improved organ integrity across all species, and extended survival in an experimental model of rat transplantation.

Conclusion
Together, our study represents a significant step forward in the field of kidney transplantation with the potential to immediately change the clinical practice. Furthermore, our discovery can be easily and cost-effectively applied in resource-constrained environments, where there is an equally pressing demand for increased transplant numbers, yet available funds for large infrastructure changes are scarce.

PV05-06

Longitudinal Dynamics Of The NK Cell Repertoire After Lung Transplantation And Their Potential Role For Control Of CMV Reactivation

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Introduction
Lung transplantation (LTx) is the ultimate option for patients suffering from end stage lung diseases. In the early postoperative period, primary graft dysfunction (PGD) is the main complication and followed years later by chronic lung allograft dysfunction (CLAD) associated with the risk of graft loss. In addition, CMV infections represent a clinically relevant complication, especially in high-risk groups of CMV- recipients of CMV+ donor lungs (D^+R^-). Since NK cells are involved in the control of

CMV infection, we studied the early dynamics of NK cell subsets in LTx recipients and their potential role for CMV reactivation/infection, PDG and CLAD.

Methods

Immune phenotyping of peripheral blood samples from n=31 LTx recipients at time points pre, T0, T24 and 3 weeks post LTx was conducted using flow cytometry. Longitudinal dynamics of NK cell subsets in LTx recipients were correlated with organ preservation (EVLP vs. SOC), PGD, CLAD and CMV reactivation.

Results

Dynamic changes in all lymphocyte subsets early after LTx are detectable. Relative NK cell frequencies increase significantly ($p<0.05$) directly post-LTx with $CD56^{dim}CD16^{high}$ as major NK subset, while cell numbers decrease simultaneously. The frequency of $HLA\text{-}DR^{+}CD56^{dim}$ NK cells increased within 3wks post LTx ($p<0.05$), indicating activation. A prominent population of terminally differentiated $CD57^{+}CD56^{dim}$ NK cells was detected already before LTx independently of age. With n=31 patients included, a tendency for increased frequencies of $HLA\text{-}DR^{+}CD57^{+}$ NK cells was observed in LTx recipients with EVLP-preserved lungs. In patients developing PGD or CLAD, differences in NK cell subsets, i.e. $CD56^{dim}CD16^{high/low}$, $HLA\text{-}DR^{+}CD57^{+/-}$ were already detectable pre-LTx. Finally, patients with CMV reactivation showed a trend for reduced frequencies of $CD56^{dim}CD16^{low}$ NK cells also arguing for a role in CMV control.

Conclusion

Memory NK cell subsets may can contribute to the control of alloreactivity as well as CMV reactivation. Hence, they could also potentially influence the development of CLAD, which needs to be substantiated in a larger cohort, we are currently working on.

Poster Session 06: Lung

PV06-01

Herpes Simplex Virus Diagnosis In The Bronchoalveolar Lavage Of Immunocompromised Patients With Lower Respiratory Tract Infections: Results Of A Prospective Study

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Introduction

Human herpes simplex virus (HSV) infections are prevalent and pose significant risk for immunocompromised (IC) individuals. This study aimed to evaluate the impact of lower respiratory infections (LRTIs) with HSV diagnosed via PCR in bronchoalveolar lavage fluid (BALF) in immunocompromised patients.

Methods

2,666 visits of 1,301 patients undergoing bronchoscopy for suspicion of LRTI were included in this study. Of these, 119 cases tested positive for HSV1 and/or HSV2 in BAL (haematological disease (n=43), solid organ transplantation (n=24) and other causes (n=52)). The primary outcome assessed was predefined modifications in patient management with follow-up conducted for up to 30 days.

Results
BAL findings prompted therapeutic adjustments in 69.19% (n=82) of HSV-infected cases. Among the 119 HSV-positive cases, 63.87% (n=76) demonstrated coinfections with viral, fungal, or bacterial pathogens. Mixed infections were associate to higher neutrophil counts in BALF (42% CI 7.5-84-5% vs. 9% CI 2-59.5%). Unadjusted 30-day mortality rates were nummerically higher in those with positive HSV PCR in BALF (9.4% vs 5.7%, p=0.0961).

Conclusion
Respiratory infections with HSV are in the majority of cases associated with coinfection with bacterial, viral or fungal pathogens. Fiberoptic bronchoscopy, including BAL, emerges as a valuable tool facilitating treatment modifications in immunocompromised patients with LRTIs associated with HSV.

PV06-02

Clinical Outcomes Of A Lung Transplant Cohort Treated With Tixagevimab/ Cilgavimab As Pre-Exposure Prophylaxis For SARS-COV-2 Infection During The Omicron BA.2 And BA.4/5 Waves

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Introduction
Lung transplant recipients (LTRs) exhibit increased susceptibility to SARS-CoV-2, affecting both short-term morbidity and mortality, with potential long-term impacts. Despite being vaccinated, these patients exhibit lower seroconversion rates, indicating a heightened risk of breakthrough infections. Pre-exposure prophylaxis (PREP) using tailored monoclonal antibodies has shown effectiveness, leading to emergency use authorization by international and local authorities early in the pandemic [1,2,3]. However, the rapid evolution of the virus has compromised the longevity of these type of treatments.

Methods
A low-risk, single-center retrospective study was conducted from April to October 2022 to evaluate the clinical and safety outcomes, and anti-spike antibody IgG levels in LTRs using tixagevimab/cilgavimab as PREP. Of 128 LTRs, 78 were eligible for this strategy based on specific clinical characteristics. Twenty-nine of them received the treatment, and 43 were selected as matched controls.

Results
The treatment group exhibited a numerical lower incidence of COVID-19 infection—17% compared to 37% in the control group, however, the small sample size precludes statistical significance. This trend was more evident in the first 66 days of treatment, with a hazard ratio of 1.670 (95% CI:0.552-5.054) favoring the treatment group. Additionally, a smaller proportion of the treatment group required hospitalization (40% vs. 75%), resulting in an odds ratio of 0.222 (0.027–1.846). The follow-up indicated significant anti-spike IgG seroconversion in the treatment group, with no major adverse reactions. The control group recorded three deaths, one directly from COVID-19.

Conclusion
Despite the rapid evolution of resistance, the study underscores the importance of PREP strategies including mAbs in reducing COVID-19 infection rates and hospitalizations among LTRs, offering additional real-world evidence of the efficacy of tixagevimab/cilgavimab during the early Omicron wave. Future PREP strategies should incorporate a multimodal approach, combining vaccination, tailored monoclonal antibodies resistant to variants, and selective antivirals, to safeguard this vulnerable population.

References

[1] **Myron J, Andrew U, Stéphane D, et al.** Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for prevention of Covid-19. N Engl J Med. 2022; 386:2188-2200. DOI: 10.1056/NEJMoa2116620

[2] **Focosi D, Casadevall A.** A Critical Analysis of the Use of Cilgavimab plus Tixagevimab Monoclonal Antibody Cocktail (Evusheld™) for COVID-19 Prophylaxis and Treatment. Viruses. 2022; 14(9):1999. https://doi.org/10.3390/v14091999

[3] **Eck D, Chapin K, Siedlecki A, et al.** Evusheld Protects Against SARS-CoV-2 in Lung Transplant Recipients. J Heart Lung Transplant. 2023 Apr;42(4). doi: 10.1016/j.healun.2023.02.1410. Epub 2023 Apr 3. PMCID: PMC10068078

PV06-03

ECG-Based Detection Of An Atrial Cardiomyopathy Allows Identification Of Patients At Risk For Postoperative Supraventricular Arrhythmias After Lung Transplant

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Introduction

Postoperative supraventricular arrhythmias (SVA) frequently occur after lung transplant (LTX) and are associated with an increased risk of morbidity and mortality. An atrial cardiomyopathy (ACM) is a known risk factor for new-onset SVA and can be detected non-invasively by measurement of the p-wave-duration on electrocardiogram (ECG). However, studies investigating the impact of ACM on the occurrence of SVAs in patients undergoing LTX are lacking.

The aim of the current study is to investigate whether ECG-based ACM-detection is associated with the risk of postoperative SVAs in patients who underwent LTX.

Methods

We retrospectively screened 134 patients who underwent first LTX at the University of Freiburg between 2014 and 2022. In 64 of these patients (median age: 60 years, 53 % male), a digital ECG prior to LTX was available and patients survival was at least one month post LTX. P-wave duration has been measured after amplification of the digital ECG to 80 mm/mV and 175 mm/s. SVAs were defined as an episode lasting >30 seconds on telemetry monitoring on intensive care unit or diagnosed in 12-lead ECG on normal ward.

Results

Postoperative SVAs occurred in 33 patients (52%) after LTX. The risk of SVAs was significantly associated with a prolonged p-wave duration with an increase of 6% with every millisecond duration (p=0.031) and remained significant after adjustment for age, sex and BMI (p=0.042).

Conclusion

Detection of an ACM diagnosed by a prolonged p-wave duration in patients undergoing LTX allows to identify patients at risk for postoperative SVAs who should be monitored more closely.

PV06-04

Clinical Outcomes For COVID-19 In Lung Transplant Recipients (LTRs): An Insight From The Early Omicron Wave

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Introduction

Early reports indicate lung transplant recipients (LTRs) face heightened COVID-19 mortality and morbidity risks, although recent data show improvement [1]. Persistent challenges include weaker vaccine responses, higher viral loads, and drug-resistant variants. Prolonged infections and potential graft damage remain critical concerns [2,3]. Rapid viral evolution, often accelerated by antivirals, has rendered treatments like monoclonal antibodies obsolete (MAbs). This study aims to investigate the short-term impact of SARS-COV-2 infection on LTRs in a real-life setting.

Methods

A low-risk, single-center retrospective observational study was conducted to evaluate clinical outcomes using data from electronic medical records from January 2022 to March 2023. Among 118 LTRs, 68 patients were diagnosed with SARS-COV-2 infection from January 2022 to March 2023, resulting in an incidence rate of 57%.

Results

This cohort with a 57% male predominance, had a mean age of 62.74 years and a BMI of 25.71. Most patients underwent double-lung transplants (97.1%) for COPD or ILD. The most common post-transplant complication was Chronic rejection (45.6%). Tacrolimus and Mycophenolate was the primary immunosuppressant regime (76.5%). Patients received a median of 3 COVID vaccine doses, with 82% showing negative titters.

Outcomes indicated a 2.9% mortality rate and 73 infection episodes. Hospital-based care was required for 53.4% of cases, with a median stay of 10 days, and ICU/NIV for 6.8%. Treatments included antiviral therapy (45%), corticosteroids (32.8%), and mAbs (32.8%). COVID-19 pneumonia occurred in 30.1% of patients, bacterial superinfection in 28.7%, and 39.7% needed changes in immunosuppressors.

Conclusion

SARS-CoV-2 infection remains prevalent in LTRs, but a trend toward lower mortality is observed when compared to the reports coming from the early pandemic. Hospitalization with prolonged stays, addition of antivirals and/or mABS is common. Older age, lower BMI, low antibody titers, and tacrolimus use, unlike tacrolimus/sirolimus combination, are statistically associated with COVID-19 pneumonia. Long-term outcomes remain uncertain, making ongoing epidemiological monitoring essential.

References

[1] **Casutt A, Papadimitriou-Olivgeris M, Ioakeim F, et al.** Outcomes of SARS-CoV-2 infection among lung transplant recipients: A single-center retrospective study. Transpl Infect Dis. 2023; 25. https://doi.org/10.1111/tid.14007

[2] **Manothummetha K, Chuleerarux N, Sanguankeo A, et al.** Immunogenicity and Risk Factors Associated With Poor Humoral Immune Response of SARS-CoV-2 Vaccines in Recipients of Solid Organ Transplant: A Systematic Review and Meta-Analysis. JAMA Netw Open. 2022; 5(4). https://doi.org/10.1001/jamanetworkopen.2022.6822

[3] **Li P, de Vries AC, Kamar N, et al.** Monitoring and managing SARS-CoV-2 evolution in immunocompromised populations. The Lancet Microbe. 2022; 3(5). https://doi.org/10.1016/S2666-5247(22)00061-1

PV06-06

Outcome Of Lung Transplant Recipients Being Previously Refused In Other Transplant Centers

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Introduction

Lung transplantation (LuTx) is a life-saving treatment option for patients with end-stage lung diseases. The decision which patients are suitable candidates for LuTx remains a clinical challenge. Refusal in one center does not necessarily imply that LuTx cannot be safely performed. We sought to analyze the outcomes of LuTx recipients who were refused in other transplant centers.

Methods

Between 09/2017 and 04/2024 we identified 13 recipients, who were previously refused in external centers but accepted in our center. In this retrospective investigation we compared the outcomes with 108 recipients, who were transplanted in the same time period.

Results

Group 1 consisted of patients (n=13, 2 bilateral LuTx, 11 unilateral LuTx, mean age 54±12 years) for whom LuTx had been refused in an external transplant center. Reasons for refusal of LuTx were comorbidities such as cachexia, obesity, ECMO, muscular deconditioning due to prolonged ICU-treatment and psychological instability. Group 2 included all other LuTx recipients (n=108, 48 bilateral LuTx, 60 unilateral LuTx, mean age 54±11 years) within the same time period. Four patients of group 1 died (COVID-19: n=2, CLAD: n=1, hypoxic brain damage: n=1). Survival was similar with 92 % vs. 83 % at 1 year and 85 % vs 74 % at 3 years (p=0.635). The development of CLAD tends to be lower in group 1 (15 % vs. 37 %, p=0.216).

Conclusion

Identification of suitable candidates for LuTx is an extreme challenge and requires high expertise of the multidisciplinary transplant team [1], [2]. Refusal in one center – irrespective of center transplant volume – does not necessarily excludes the patient from life-saving LuTx. Successful outcomes can be achieved despite previous refusal judgements.

References

[1] Leard LE, Holm AM, Valapour M, Glanville AR, Attawar S, Aversa M, Campos SV, Christon LM, Cypel M, Dellgren G, Hartwig MG, Kapnadak SG, Kolaitis NA, Kotloff RM, Patterson CM, Shlobin OA, Smith PJ, Solé A, Solomon M, Weill D, Wijsenbeek MS, Willemse BWM, Arcasoy SM, Ramos KJ. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2021 Nov;40(11):1349-1379

[2] Verleden GM, Dupont L, Yserbyt J, Schaevers V, Van Raemdonck D, Neyrinck A, Vos R. Recipient selection process and listing for lung transplantation. J Thorac Dis. 2017 Sep;9(9):3372-3384.

PV06-07

Diagnosis Of Cytomegalovirus In BALF Of Immunocompromised Patients And Its Association With Outcome

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Introduction
Cytomegalovirus is a common virus that can affect individuals across all age groups. While individuals with a healthy immune system may experience no symptoms during a cytomegalovirus infection, it may cause severe disease or even be life-threatening in immunocompromised patients. This study aimed to evaluate the impact of lower respiratory tract infections (LRTIs) caused by CMV, as diagnosed through polymerase chain reaction (PCR) testing of bronchoalveolar lavage fluid (BALF).

Methods
2,666 visits involving 1,301 immunocompromised patients with symptoms of LRTI underwent diagnostic BAL, with 235 cases testing PCR positive for CMV in BALF. Main diagnosis were haematological (n=88), solid organ transplantation (n=70), and other forms of immunosuppression (n=77). The primary composite outcome encompassed predefined modifications in patient management within 30 days following bronchoscopy.

Results
Overall 59 cases exhibited isolated CMV infection, while 176 displayed coinfections. Isolated CMV infection was associated with more macrophages in BALF (75.5%, CI: 44.0 – 85.0). Coinfection was associated with neutrophilia in BALF (haematological 23.25% CI: 4.25-67.0; others 35.00%, CI 10.0-65.00). BAL findings prompted treatment modifications in 61.7% (n=145) of all CMV-BALF positive cases. The 30-day mortality rate stood at 13.6%, with a significantly elevated hazard ratio for those with CMV-positive BAL PCR diagnosis (unadjusted HR 2.85, 95%CI: 1.86-4.36,).

Conclusion
This study underscores the pivotal role of bronchoscopy with BAL in altering the management of immunocompromised patients with CMV-related infections, with mortality risk nearly tripling in patients with a positive CMV PCR in BAL fluid.

PV06-08

Ten-Year Experience With Peritransplant Desensitization In Patients With Preformed Donor Specific Antibodies In Lung Transplantation

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Introduction
Pretransplant sensitization to human leukocyte antigens (HLA) increases the recipient waiting list time and mortality in lung transplantation. Instead of awaiting crossmatch-negative donors, since 2013, recipients with preformed anti-HLA donor specific antibodies (pfDSA) have been managed peri-transplant at our institution with a combination of repeated IgA- and IgM-enriched intravenous immunoglobulin infusions (IgGAM, first infusion: 2gr/kg, then 0.5gr/kg every 4 weeks thereafter to a maximum of 6 months), preceded by repeated plasmapheresis (PE), and a single dose of anti-CD20 antibody (375mg/m^2, Rituximab) after the first IgGAM infusion.

Methods
Records of patients transplanted at our institution between 02/2013 and 02/2024 were reviewed. Outcomes were

compared between patients with pfDSA (pfDSA group) and those without any early DSA (eDSA-, control group). Patients without pfDSA who developed DSA only post transplantation (n=242) were excluded from the analysis. Median follow-up was 55 (21 - 90) months.

Results

Of the 1167 transplanted patients,69 (6%) patients exhibited pfDSA and 857 (73%) did not develop any DSA (control group). Among these 69 patients, 43 (62%) patients possessed pfDSA against class II HLA antigens, 20 (29%) patients against class I antigens, and 6 (9%) patients against both classes. Thirteen (19%) patients showed a positive retrospective CDC crossmatch and 23 (33%) patients developed additional de-novo DSA after transplantation. At end of follow-up, treatment was completed in 59 (85%) patients. In these patients, IgGAM treatment cleared DSA in 43 (73%) patients, with 10 (23%) patients showing DSA recurrence. In pfDSA vs. control patients, prevalence of primary graft dysfunction grade 3 at 72 hours was 10.1% vs. 4.3% (p=0.038). However, graft survival (%) and freedom from chronic lung allograft dysfunction (%) did not differ between groups (at 9 years, 68 vs. 60, p=0.79; 64 vs. 67, p=0.61), respectively.

Conclusion

In lung transplantation, a peritransplant desensitization protocol allowed transplanting patients with pfDSA with good 10-year graft survival similar to control patients.

Author Index

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z

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