Transplant International

AUSTROTRANSPLANT

Austrotransplant 2025: Transcending Boundaries – Unveiling the Shared Knowledge and Experience in Transplantation

Transplant International

frontiers | Publishing Partnerships

Introduction

Dear Sir or Madam,
Dear Colleagues,

It is a special honor and pleasure for us to welcome you to this year's annual meeting of the Austrian Society for Transplantation, Transfusion and Genetics – "AUSTROTRANSPLANT" in Schladming.

The organizing committee is pleased to offer you, once again this year, exciting insights into current developments and topics in the field of transplantation – both in terms of solid organ transplantation and stem cell transplantation – in a compact three-day period.

The theme of this year's annual meeting is "Transcending Boundaries: Unveiling the Shared Knowledge and Experience in Transplantation." This theme reflects the ongoing exchange and collaboration across geographical, cultural, and disciplinary boundaries. Through increased dialogue and knowledge sharing, we can jointly develop innovative solutions and new perspectives on the challenges of transplantation.

The growing discrepancy between the demand for organs and the available supply challenges us to continuously research and develop creative solutions. There will be opportunities to address significant developments in plenary sessions and to engage in in-depth discussions in topic-specific parallel sessions. We will also once again offer poster sessions, providing a space for intensive exchange and discussion.

A particular concern of the Society is the promotion of young researchers in the field of transplantation. For this reason, several prizes will be awarded during the meeting, which will be presented in a separate Young Researcher session.

Another highlight of the AUSTROTRANSPLANT Annual Conference is this year's nursing conference, which is specifically geared toward nurses from transplant centers. The goal is to create a platform for mutual exchange and the further development of collaboration.

Finally, we would like to sincerely thank the industry for their generous support, without which the conference would not be possible.

The organizing committee cordially welcomes you to Schladming and hopes to welcome you to the AUSTROTRANSPLANT Annual Conference in October.

Robert Sucher (Conference President)
Philipp Stiegler (Conference Secretary)

Table of contents

Marlena Buresch[1],
Moritz Muckenhuber[1], Verena Kainz[1],
Heinz Regele[2] and
Thomas Wekerle[1]

[1] Medical University of Vienna,
 Dept. of General Surgery, Div. of
 Transplantation
[2] Medical University of Vienna,
 Clinical Institute of Pathology

01

Costimulation-Independent Secretion Of IgM DSA By Marginal Zone B Cells

Background

Costimulation blockade with CTLA4-Ig/belatacept reduced the incidence of IgG donor-specific antibodies (DSA) in kidney transplantation compared to standard of care calcineurin-inhibitors. However, a notable fraction of patients on belatacept develop IgM-DSA, indicating that a distinct form of B-cell allo-immune response persists under costimulation blockade. This project aimed to characterize the nature of these costimulation-independent B cell responses and their consequence for transplantation in a mouse model for cardiac transplantation.

Methods

CCR5 knock-out mice (CCR5KO; C57BL/6 background, H-2b), which exhibit pronounced humoral allo-immunity, received fully mismatched BALB/c (H-2d) cardiac allograft under CTLA4-Ig monotherapy (1.25mg/dose on days 0, 4, 14, 28, 54, 86) and were followed for up to 100 days. Donor reactive B cell subsets were identified via flow cytometry using recombinant donor MHC tetramers. DSA were quantified via ELISA.

Results

CTLA4-Ig prolonged graft survival (MST >100 days) in CCR5KO mice receiving BALB/c cardiac allografts, preventing IgG but not IgM-DSA formation, modeling the clinical situation. Bone marrow, spleen, and lymph node cells isolated from CTLA4-Ig treated cardiac allograft recipients 21 days post-transplantation were cultured separately. An ELISA of the culture supernatants identified the spleen as primary source for costimulation-independent IgM-DSA. To identify the cellular source of IgM-DSA, we tracked donor-reactive IgM$^+$ B cells in recipient spleens using fluorophore-conjugated recombinant donor MHC tetramers. We found that IgM$^+$ donor-reactive B cells predominantly display a marginal zone B cell phenotype (CD1d$^+$CD21^{high}). Interestingly, CTLA4-Ig abrogated the formation of donor reactive germinal centers, while the number of donor-reactive marginal zone B cells remained unaffected. Cultivation of sorted B cell subsets identified plasmablasts (CD138$^+$CD19$^+$) as primary source for the extrafollicular IgM-DSA

under CTLA4Ig treatment, consistent with findings showing that extrafollicular marginal zone B cells can differentiate into short-lived antibody-secreting plasmablasts.

Conclusion

These findings suggest that marginal zone B cells can differentiate into IgM-DSA secreting plasmablasts despite costimulation blockade.

First Series Of A Nature-Inspired Subzero Kidney Preservation And Transport Abroad A Commercial Transatlantic Flight

Anne Heberle[1], Amanda H. Loftin[2], Marlene Pühringer[1], Julia Hofmann[1], Theresa Hautz[1], Stefan Schneeberger[1], Eleni Drivas[2], Siavash Khaki[2], Narges Lamsehchi[2], Xiaoxi Wei[3], Mark Kline[3], Byoung Chol Oh[2], Gerald Brandacher[1,2]

[1] Department of Visceral, Transplant and Thoracic Surgery, OrganLife® Laboratory, Medical University of Innsbruck, Innsbruck, Austria
[2] Department of Plastic and Reconstructive Surgery, Vascularized Composite Allotransplantation Laboratory, Johns Hopkins University School of Medicine, Baltimore, MD, US
[3] X-Therma Inc., Hercules, CA

Background

The global demand for transplantable organs has increased. Subzero strategies may extend organ preservation and enhance the possibility of global transport. This study investigates the feasibility of an organ preservation solution containing a nature-inspired anti-icing agent, called XT-ViVo®, and the organ transporter TimeSeal® for commercial transatlantic flight transports.

Methods

Porcine Kidneys were retrieved in Baltimore (USA), flushed with XT-ViVo®, stored at -5°C, and transported in the TimeSeal® via plane to Innsbruck (Europe). Following Subzero Storage (19.5-72.5 hours), assessment of graft function was conducted by 6 hours of Normothermic Machine Perfusion (NMP) using the Kidney Assist (Organ Assist, Groningen). To verify organ integrity, viability, and evaluate mitochondrial activity via high-resolution respirometry (HRR), biopsies were collected before, during, and after NMP. Additionally, perfusate and urine samples were collected for biochemical analysis. Microperfusion was assessed using hyperspectral imaging (HSI).

Results

The TimeSeal® organ transporter maintained temperature at -5.3 °C $\pm$ 0.44°C during subzero storage consistently. During NMP, kidneys exhibited stable hemodynamic flow (130.9 mL/min [117.5−140.5]; median [IQR]), continuous urine output (253.2 mL/h [178.4−339.6]), and a renal resistance index of 0.6. All kidneys demonstrated moderate oxygen consumption, peaking after two hours of reperfusion (22 mL O_2/min/100 g [12.4−28.6]), followed by a decline toward the end of NMP (15 mL O_2/min/100 g [11.8−16.6]). Physiological pH levels, moderate perfusate lactate concentrations (26 mg/dL [18-52]), and ion levels were observed. HRR measurements indicated succinate as the primary substrate pathway and revealed a decline in OXPHOS capacity and ATP production efficiency, accompanied by an increase in outer mitochondrial damage towards the end of perfusion. HSI confirmed consistent perfusion throughout the 6-hour NMP period.

Conclusion

Ice-free subzero preservation combined with NMP may represent a promising and clinically translatable approach for safe global organ transport.

CXCR3+ Tissue-Resident Memory T Cells Correlate With Protection From Keratinocyte Cancer In Organ Transplant Recipients

Konrad Chrapla[1], Liliane Borik-Heil[1], Bärbel Reininger[1], Simona Saluzzo[1], Georg Stary[1,2]

[1] Department of Dermatology, Medical University of Vienna; Vienna, 1090, Austria
[2] CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences; 1090 Vienna, Austria

Background

Organ transplant recipients (OTRs) require lifelong systemic immunosuppressive therapy (SIT), substantially increasing their risk for keratinocyte cancers (KC) such as cutaneous squamous cell carcinoma. Interestingly, not all OTRs develop KC despite SIT, suggesting individual variation in skin-specific immune defense. Tissue-resident memory T cells (TRMs), especially CD8^{+}CXCR3^{+} subsets, are known to play a crucial role in antiviral and antitumor immunity. This study investigates whether TRM composition in the skin correlates with natural protection against KC in OTRs.

Methods

We analyzed skin biopsies from matched OTR cohorts composed of OTR patients with >5 histologically confirmed KC (OTR[KC]) and OTR that were naturally protected from KCs (OTR[PRO]) without KC in the post-transplant period. Patients were matched for years of post-transplant period, age, gender, SIT medications, and cumulative sun exposure. A 6 mm punch biopsy was obtained from the inner upper arm, and processed for multicolor immunofluorescence staining for CD3, CD4, CD8, CD69, and CXCR3. Quantification of TRMs in the skin was performed using TissueFAXS and TissueQuest imaging systems.

Results

CXCR3^{+}CD4^{+} TRMs were more abundant in the skin of healthy controls compared to both OTR groups. Notably, a clear trend toward higher numbers of CXCR3^{+}CD4^{+} TRMs was observed in OTRs protected from KC compared to KC-susceptible patients. CXCR3^{+}CD8^{+} TRMs were significantly higher in OTR[PRO] relative to OTR[KC] (p = 0.0028), indicating a potential role for this subset in mediating local tumor immune surveillance under immunosuppression.

Conclusion

Our findings highlight a potential protective role of skin-resident CD8^{+}CXCR3^{+} TRMs in preventing KC in immunosuppressed individuals. This subset may serve as a predictive biomarker for skin cancer risk in OTRs. Therapeutic strategies to preserve or restore these cells could reduce KC incidence in vulnerable populations. These insights may extend beyond OTRs, offering broader relevance for cutaneous cancer prevention.

Liver Preservation For Seven Days Using A Fully Automated Normothermic Machine Perfusion Device And The Innsbruck Perfusion Protocol

Julia Hofmann[1], Christina Bogensperger[1], Andras T. Meszaros[1], Madita L. Buch[1], Florian Nardin[1], Benno Cardini[1], Bettina Zelger[2], Martin Hermann[1,3], Margot Fodor[1], Franka Messner[1], Fabian Scherbauer[1], Magdalena Bordt[1], Felix J. Krendl[1], Hannah Esser[1], Silvia Oberparleiter[1], Valeria Berchtold[1], Marlene Pühringer[1], Simon Mathis[3], Gabriel Putzer[3], Andrea Griesmacher[4], Christian Irsara[4], Harald Schennach[5], Judith Martini[3], Stefan Scheidl[1], Christian Margreiter[1], Manuel Maglione[1], Annemarie Weissenbacher[1], Rupert Oberhuber[1], Dietmar Öfner[1], Jakob Troppmair[1], Thomas Resch[1], Theresa Hautz[1], Stefan Schneeberger[1]

[1] organLife Organ Regeneration Center of Excellence, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, 6020 Innsbruck, Austria
[2] Institute of Pathology, Neuropathology and Molecular Pathology, Medical University of Innsbruck, Innsbruck, Austria
[3] Department of Anesthesia and Critical Care Medicine, Medical University of Innsbruck, Innsbruck, Austria
[4] Central Institute of Medical and Chemical Laboratory Diagnostics, University Hospital of Innsbruck, Innsbruck, Austria
[5] Central Institute for Blood Transfusion and Immunological Department, University Hospital of Innsbruck, Innsbruck, Austria

Background

While short (24 hours) normothermic machine perfusion (NMP) is applied to assess livers prior to transplantation, prolonged NMP offers the potential for modification, regeneration, and repair of marginal grafts. We aimed to establish a clinically applicable protocol for long-term NMP (Innsbruck perfusion protocol).

Methods

Livers retrieved from domestic pigs (N=18) were perfused for up-to 7 days using a commercially available system (OrganOx Metra®). A precision-cut liver slice culture model was applied to assess and determine the perfusate recipe. The perfusion protocol was assessed and validated in a stepwise process and later evaluated in non-transplanted human livers (N=22).

Results

In porcine experiments, unmodified perfusion resulted in progressive deterioration of liver grafts after 48 hours NMP. The stepwise development of a novel perfusion protocol including daily substitution with donor-derived whole blood to compensate for the volume loss related to bile excretion prolonged liver viability beyond 72 hours. After refinements including modification of bile excretion and expansion of the anti-infective therapy, stable function and morphological integrity of porcine livers after 7-day perfusion was achieved. Application of Innsbruck perfusion protocol in non- transplanted human livers resulted in long-term perfusion 135[98 – 166] hours, while full 7-day perfusion was achieved in livers with lower degree of pre-existing damage. These grafts showed well- preserved viability and bioenergetic function along with continuous bile production, low perfusate bilirubin and methemoglobin levels at day 7. A cause-effect analysis indicates that free hemoglobin release seems crucial for a successful 7-day perfusion, along with low interleukin-6 levels.

Conclusion

7-day preservation of porcine and human livers using the Innsbruck perfusion protocol in a fully automated commercial perfusion system is feasible.

Non-Invasive Quantification Of Urinary VP1-Positive Epithelial Cells: Towards A Liquid Biopsy Standard For BKPyVAN

Haris Omic[1], David Vescei[1], Michael Eder[1], Karim Abd El-Ghany[1], Wolfgang Winnicki[1], Alice Schmidt[1], Sebastian Kapps[1], Daniela Gerges[1], Robert Strassl[2], Ludwig Wagner[1] and Farsad Eskandary[1]

[1]Department of Medicine III, Division of Nephrology and Dialysis, Medical University of Vienna, Vienna, Austria
[2]Department of Clinical Virology, Medical University of Vienna, Vienna, Austria

Introduction

Intense immunosuppression after kidney transplantation may cause polyomavirus nephropathy (BKPyVAN) and contribute to allograft dysfunction and loss. Quantitative PCR is the current gold standard for its detection, but may not always reflect tissue damage. We investigated a novel non-invasive approach based on the quantification of viral capsid protein 1 (VP1) in urinary epithelial cells, which may reflect ongoing tubular cell damage more reliably.

Methods

This observational cohort study encompassed 30 kidney-transplant recipients with BK polyomavirus (BKPyV) reactivation. Urine samples were analyzed by fluorescence-assisted cell sorting (FACS) using a rabbit polyclonal anti-VP1 antibody to quantify VP1-positive reno-urinary epithelia.

Results

At baseline, median urinary VP1-positivity was significantly higher in biopsy-proven BKPyVAN (33.0%, IQR 26.5-45.8) vs. non-BKPyVAN patients (4.5%, IQR 1.2-12.7; $p<0.001$). ROC analysis yielded an AUC of 0.90 (95%

CI 0.80-1.00) for detecting biopsy-proven BKPyVAN; a 17.5% VP1 cut-off achieved 81.8% sensitivity and 84.2 % specificity. Leave-one out cross validation (LOOCV) produced an AUC of 0.88 (95% CI 0.75-1.00). Longitudinally, median VP1 burden declined from 12.7% (IQR 3.9-29.3) at baseline to 0% (IQR 0-0.9), with the steepest drop between months two and four (p<0.05). In contrast, plasma BKPyV-DNAemia showed an early rapid decline, but plateaued at ~4×10^2 to 7×10^2 copies/mL. Mixed-effects modeling estimated a 4% weekly decline in VP1 positivity (exp β=0.96; p=0.047).

Discussion

Besides plasma PCR as the gold-standard, urinary liquid biopsies using VP1 flow-cytometry may offer an adjunctive quantitative assessment of ongoing BKPyV replication within the reno-urinary tract. Our preliminary results suggest that using this method in combination with plasma PCR, BKPyVAN severity tiers can be distinguished with considerable accuracy, and longitudinal measurement may allow for an earlier detection of viral resolution compared to using DNAemia alone. Its implementation in post-transplant surveillance might have the potential to support the decision-making process of when to re-establish appropriate maintenance immunosuppression levels.

06

Enteric PROMs In Pediatric Kidney Transplant Recipients May Be Linked To Chronic Allograft Dysfunction By Gut Microbiome Dysbiosis

Fabian Eibensteiner[1], Valentin Ritschl[2], Krisztina Heindl-Rusai[1], Thomas Mueller-Sacherer[1], Christoph Aufricht[1], Michael Boehm[1]

[1] Division of Pediatric Nephrology and Gastroenterology, Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria
[2] Institute for Outcomes Research, Center for Medical Data Science, Medical University of Vienna, Vienna, Austria

Background

Post-transplant diarrhea (PTD) is a frequent but neglected complication of kidney transplantation (KTX). We previously identified enteric patient-reported outcome measures (PROMs) to be associated with allograft dysfunction in pediatric KTX. While investigations in adults highlight the potential role of gut dysbiosis in development of PTD, pediatric studies are missing. Here we investigated the association between gut microbiome, PROMs, and allograft function in pediatric KTX.

Methods

This was a prospective observational pilot study in pediatric KTX recipients at the Medical University of Vienna. PROM questionnaires and fecal samples were collected cross-sectional at regular outpatient clinic visits. Fecal samples were analyzed with metagenomic shotgun sequencing. Taxonomies and metabolic pathways were identified using Metaphlan and Humann. Group comparisons were calculated with Mann Whitney U and PERMANOVA tests (alpha and beta diversity) and ANCOM-BC II (individual species and metabolic pathways).

Results

16 KTX recipients, at median 15 years (IQR 12-17), 4.7 years after KTX (IQR 1.3-13.8), 10 male, with 11 deceased donations, and 13 on their first allograft were included in this study. PTD was present in 4 patients. Alpha diversity was significantly lower in patients with PTD (p=0.02) while beta diversity did not differ. In PTD Clostridium innocuum (p=0.0016) and Bacteroides xylanisolvens (p=0.038), among others, significantly increased while Faecalibacillus intestinalis (p=0.038) and nucleotide synthesis (p=0.004) was significantly reduced. Higher abundance of C. innocuum was further significantly associated with worse allograft function (p=0.045), amount of nucleotide synthesis with FK trough levels (p=0.066).

Conclusions

Clostridiales have been associated with Tacrolimus inactivation in vitro, thereby C. innocuum increase alongside reduced nucleotide synthesis (i.e., DNA damage repair) may potentially link PTD to worse allograft outcomes

in pediatric KTX recipients. For the first time we herein demonstrated the potential benefits of PROM assessment in pediatric KTX recipients strengthened by a pathobiological basis.

07

Allograft Tolerance May Be Linked To The Endogenous Self-Peptide Repertoire Bound To Allogeneic MHC I In Pediatric Kidney Transplant Recipients

Fabian Eibensteiner[1], Krisztina Heindl-Rusai[1], Rebecca Herzog[1], Thomas Mueller-Sacherer[1], Christoph Aufricht[1], Nina Pilat[2,3], Klaus Kratochwill[1,4]

[1] Division of Pediatric Nephrology and Gastroenterology, Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria
[2] Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria
[3] Center for Biomedical Research and Translational Surgery, Medical University of Vienna, Vienna, Austria
[4] Core Facility Proteomics, Medical University of Vienna, Vienna, Austria

Background

Rejection and adverse effects of immunosuppression limit long-term allograft and patient survival. With 10-year graft survival of 61-77%, pediatric kidney transplant (KTX) recipients require multiple allografts throughout their lifetime. Tolerance, without the need for immunosuppression, would solve this. In mice, tolerance is dependent on endogenous self-peptides presented by allogeneic MHC I. Here we investigated tolerance signatures within the plasma self-peptide repertoire of pediatric KTX recipients.

Methods

This was a prospective observational study in pediatric KTX recipients at the Medical University of Vienna. The plasma proteome was measured via mass spectrometry (Orbitrap Exploris 480, DIA). Potential tolerance was defined as unusually low immunosuppression without alloimmune events during follow-up. MHC binding-strength for each protein was calculated using netMHCpan and high-resolution HLA typing. Differential abundance and associations were calculated using LIMMA and spearman correlation.

Results

3 potentially tolerant and 4 control KTX recipients, matched for number of HLA-mismatches, at median 15 years old (IQR 12-16), 6.7 years post-KTX (IQR 5.9-7.2), with 57% deceased donations, HLA-mismatch 3 (IQR 2-3), 90% triple immunosuppression were included. We identified 395 significantly increased (FDR $p<0.05$) vs 509 decreased plasma proteins with high binding-strength to their mismatched allogeneic donor HLA I molecules in potentially tolerant patients (e.g., ALDOB, RPS18, RACK1). Enrichment analysis of these proteins showed increased amide metabolism. 31 proteins negatively correlated ($p<0.01$) with tacrolimus trough levels (e.g., HOOK3).

Conclusions

In potentially tolerant pediatric KTX recipients, for the first time in humans, we identified a plasma protein signature based on the self-peptide repertoire with binding-capacity to mismatched donor HLA I. Proteins of this signature were found in tolerized murine kidneys (ALDO, RPS18), identified as key regulators of T-cell homeostasis (RACK1), Treg differentiation (amide metabolism), and in graft-vs-host-disease (HOOK3). This plasma signature compromises the first evidence to guide future interventional trials to achieve operational tolerance in pediatric KTX.

Cost-Effectiveness Of Hypothermic Oxygenated Machine Perfusion Compared To Static Cold Storage In The Austrian Healthcare System

Jule Dingfelder[1,2], Laurin Rauter[1], David Pereyra[1,2], Jakob Mayr[1], Flavio Müller[1], Felix Hammer-Purgstall[1], Monika Aiad[1], Thomas Soliman[1], Gabriela Berlakovich[1], Georg Györi[1]

[1]Department of General Surgery, Division of Transplantation, Medical University of Vienna, Vienna, Austria
[2]Department of General Surgery, Division of Visceral Surgery, Medical University of Vienna, Vienna, Austria

Background

Hypothermic oxygenated machine perfusion (HOPE) is known to improve outcome after liver transplantation. Its economic impact within the Austrian healthcare framework remains unknown. This study evaluates the cost-effectiveness of HOPE compared to static cold storage (SCS) in the Austrian LKF (Leistungsorientierte Krankenanstaltenfinanzierung) reimbursement system.

Methods

This retrospective analysis included 257 liver grafts that were transplanted between May 2018 and December 2024. HOPE was implemented as standard preservation method at our center in 2018. Cost of disposables and perfusion solution was calculated based on in-house prices during 2021 (3900 € and 180 €). Cost of the LiverAssist was calculated proportionally based on the life period of 7 years and average use per year (about 864€ per perfusion). In 2021, one LKF point was equivalent to 1.125 €.

Results

There was no difference in total LKF points between both groups (p=0.154), the HOPE group however scored less points attributed to additional interventions (p=0.014) and scoring of reduced points due to prolonged hospital stay (p=0.04) occurred less frequent. Length of intensive care unit stay (ICU) was comparable (p=0.847) but length of total stay was shorter in the HOPE group 19 (15-29) vs. 25 (18-46), p=0.015. Based on costs attributed to ICU stay, on average 2034 € more in the SCS group, and on costs attributed to additional interventions, on average 6688 € more in the SCS group, savings through use of HOPE is estimated at about 3548 € per patient.

Conclusions

Despite higher procedure costs associated with HOPE, lower LKF points attributed to intervention costs and ICU stay translates into an estimated saving of costs of approximately €3.548 per patient in the HOPE cohort. This encourages routine implementation of HOPE before transplantation.

02_Basic Science

ATG Mediated MZB Activation Might Promote DSA Development

Jeremias Weninger[1], Moritz Muckenhuber[1], Panagiotis Parsonidis[1], Konstantinos Mengrelis[1], Verena Kainz[1], Thomas Wekerle[1]

[1] Medical University of Vienna, Dep. of General Surgery, Division of Transplantation

Background

Anti-thymocyte-globulin (ATG) is commonly used as T-cell depleting induction in solid organ transplantation. However, recent reports suggest that ATG may paradoxically promote the formation of donor-specific antibodies (DSA). The mechanisms behind this observation are unclear. Herein, we therefore investigate the impact of ATG on B-cell activation in a translational approach.

Methods

Expression of activation markers CD86, MHC-II and CD40 on various B cell subsets was assessed via flow cytometry in: (1) peripheral blood of patients receiving ATG (Thymoglobuline®) induction 14 days before kidney transplantation as part of an ongoing clinical trial (EudraCT Nr 2018-003142-16), (2) human spleen tissue incubated with ATG and (3) murine spleens collected 6, 12, 24 and 48 hours following injection of a mouse-specific ATG preparation. Additionally, serum levels of 65 cytokines were measured longitudinally in patients upon ATG infusion using a multiplex assay.

Results

ATG was detectable on virtually all peripheral blood B cells following infusion in patients as monotherapy (14 days before the scheduled kidney transplantation) and led to an immediate upregulation of the activation marker CD86 on B cells within 12 hours. Further, it led to increased serum levels of pro-inflammatory IL-6 and TNFα early after infusion. In vitro experiments employing human spleen samples showed that within the B cell compartment, ATG primarily activates marginal zone B cells (MZB), rather than follicular B cells. Cultures of purified MZB showed that this effect is mediated directly via ATG-binding. To investigate the impact of ATG on MZB in vivo, we produced a mouse-specific ATG formulation. In this model, ATG similarly caused activation of splenic MZB in vivo.

Conclusion

Collectively, these data demonstrate that ATG directly activates MZB both in vitro and in vivo. Ongoing experiments aim to determine the implications of this effect on the survival of solid organ transplants.

Regulatory T Cell–Mediated Tolerance In Heart Transplantation: A Targeted In Vivo Expansion Approach

Laurenz Wolner[1], Romy Steiner[1], Johan William-Olsson[1], Attila Kiss[1], Andreas Zuckermann[2], Bruno Podesser[1], Nina Pilat[1,2]

[1]Center for Biomedical Research and Translational Surgery, Medical University of Vienna, Austria
[2]Department of Cardiac Surgery, Medical University of Vienna, Austria

Background

Chronic antibody-mediated rejection and cardiac allograft vasculopathy remain among the leading causes of late graft failure, with no targeted therapies currently available. Regulatory T cells (Tregs) play a central role in maintaining immune homeostasis and their therapeutic expansion is a promising strategy to promote immunological tolerance. Selective in vivo expansion of Tregs can be achieved using interleukin-2 (IL-2) complexed with a anti-IL-2 monoclonal antibody (IL-2cplx). This study aimed to evaluate the potential of IL-2cplx-based immunomodulation to induce tolerance in a murine model of heart transplantation.

Methods

Fully MHC-mismatched heart transplants were performed from BALB/c female donors into C57BL/6 recipients. Mice were treated with a combination of IL-2cplx and rapamycin on days -3, -2, and -1, followed by thrice-weekly administrations through day 29. Additionally, short-term anti-IL-6 therapy was administered (on day -1, 4 and 6). Cardiac allograft survival was assessed by palpation scoring. Donor-specific antibodies (DSA) were evaluated using flow cytometric (FACS) crossmatch assays.

Results

Treatment with the IL-2cplx protocol resulted in indefinite allograft survival (>150 days), in contrast to untreated controls (7.5 days). IL-2cplx-based therapy prevented the formation of donor-specific IgG antibodies and reduced

the donor specific T-cell response. Moreover, histology revealed lower rejection grades and less necrosis. In recipients that are presensitized against donor antigens, the IL-2cplx protocol could significantly prolong allograft survival. We could also show a shift in macrophage polarization and reduced neutrophil infiltration into the heart early after transplantation.

Conclusions

This study demonstrates that selective in vivo expansion of Tregs via the IL-2cplx protocol induces operational tolerance in a clinically relevant model of heart transplantation. Treated recipients showed significantly reduced levels of DSAs and no donor-specific T-cell response. The potency of the treatment was also verified in presensitized recipients.

These findings indicate that IL-2cplx-based immunomodulation promotes durable immune tolerance without the need for chronic immunosuppression.

11

Enhancing Post-Transplant Care In Austria: A Survey Of Primary Care Physicians' Needs And The Potential For Integrated Care Software

Angelika Rzepka[1], Kristina Reiter[2], Elisabeth Kletz[3], Sabine Koller[3], Susanna Trummer[3], Moritz Kniepeiss[3], Günter Schreier[1], Gerald Sendlhofer[4], Robert Sucher[3], Daniela Kniepeiss[3]

[1] AIT Austrian Institute of Technology GmbH, Digital Health Information Systems Center for Health & Bioresources, Graz
[2] Telbiomed Medizintechnik und IT Service GmbH, Graz
[3] Department for General, Visceral and Transplant Surgery, Medical University of Graz
[4] Research Unit for Safety and Sustainability in Healthcare, c/o Department for Plastic, Aesthetic and Reconstructive Surgery, Medical University of Graz

Background

Aftercare for transplant patients is critical for long-term success. Integrating primary care physicians (PCPs) in post-transplant management helps free up hospital resources. This study examines the challenges and support needs of Austrian PCPs in transplant aftercare, aiming to establish a network of transplant-friendly primary care practices. It emphasizes the potential of integrated care software (ICS) for improved communication between PCPs and transplant wards.

Methods

A cross-sectional survey was conducted among 85 PCPs across Austria to assess their challenges in managing transplant patients. Survey questions addressed perceived barriers to adequate care and the level of support required from transplant centers. The survey also explored PCPs' attitudes towards using ICS for enhanced communication. Data were analyzed using descriptive statistics, identifying common issues such as communication gaps and managing complex medication regimens.

Results

Nearly half (49.4%) of PCPs reported insufficient professional experience and competence in specialized transplant aftercare. Ninety percent believed a telemedical aftercare app would assist in treating transplant patients. Preferences for support tools included simple aftercare recommendations (82.2%), comprehensive medication information (83.6%), well-prepared lab values with history (65.8%), reminders for recommended exams (79.5%), and task lists for better exam management (83.6%). Additionally, PCPs expressed a need for close cooperation with transplant centers, focusing on accessible colleagues (91.3%), better information exchange (89.9%), clear therapy plans (87.5%), and structured aftercare schedules (91.3%). Only 44% had experience with ICS.

Conclusions

The results underscore a pressing need for improved information access and structured support to enhance transplant patient management. A network of transplant-friendly PCPs, supported by ICS, could enhance communication with transplant centers, fostering more coordinated care. Future efforts should prioritize clear therapy plans and structured aftercare schedules.

Digital Support Of Post-Transplant Care Using The Txmobile App – Feasibility, Acceptance, And Usage Experiences Among Older Patients

Angelika Rzepka[1], Kristina Reiter[2], Elisabeth Kletz[3], Sabine Koller[3], Susanna Trummer[3], Moritz Kniepeiss[3], Günter Schreier[1], Robert Sucher[3], Daniela Kniepeiss[3]

[1] AIT Austrian Institute of Technology GmbH, Digital Health Information Systems, Center for Health & Bioresources, Graz
[2] Telbiomed Medizintechnik und IT Service GmbH, Graz
[3] Department for General, Visceral and Transplant Surgery, Medical University of Graz

Background
Post-transplant care requires continuous and closely coordinated follow-up to detect complications early and tailor therapy accordingly. Mobile health (mHealth) applications hold promise for optimizing this process. This pilot study evaluated the feasibility and acceptance of the TXMobile app to support follow-up care for transplant patients.

Methods
A prospective pilot study was conducted with transplant recipients, who first completed a standardized baseline questionnaire assessing previous use of health apps, attitudes toward digital health solutions, and technological proficiency. Participants then used the TXMobile app for eight weeks to document vital signs, medication intake, and symptoms on a daily basis.

Results
The study included 140 participants, most of whom were over 55 years old and had completed lower secondary education. Baseline results revealed that younger patients had more experience using health apps, while older patients ($\geq$ 65 years) reported little prior use of transplant-related digital tools. However, a significant proportion of older participants already regularly documented their vital parameters, indicating strong potential for enhanced digital support in this age group.

Conclusion
The findings suggest that the TXMobile app offers substantial potential for improving transplant follow-up care, particularly among older patients. Although they had limited experience with specialized apps, their existing routines of vital parameter documentation provide a solid basis for adopting digital support tools. The baseline assessment enabled a differentiated understanding of acceptance and needs, facilitating targeted implementation of the TXMobile app. Overall, the solution supports patient-centered care and early detection of potential complications.

References
Murray KR et al. (2021). *JMIR Res Protoc*, 10(10): e26816. doi:10.2196/26816

Andrä M et al. (2022). *Digital Health*, 8: 20552076221145855. doi:10.1177/20552076221145855

Langarizadeh M et al. (2023). *BMC Health Serv Res*, 23(1): 974. doi:10.1186/s12913-023-09989-1

Employing Normothermic Liver Machine Perfusion To Model And Deliver Tumour-Targeted Therapies Ex-Situ

Alexander Kofler[1], Felix J. Krendl[1], Florian Blum[2], Benno Cardini[1], Julia Hofmann[1], Michael Guenther[3], Steffen Ormanns[3], Martin Hermann[1], Heinz Zoller[4,5], Theresa Hautz[1], Stefan Schneeberger[1], Heribert Stoiber[2], Rupert Oberhuber[1]

[1]OrganLife Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Center for Operative Medicine, Medical University of Innsbruck, Austria

[2]Institute of Virology, Medical University of Innsbruck, Austria

[3]Innpath GmbH, Tirol Kliniken, Innsbruck, Austria

[4]Department of Internal Medicine I, Medical University of Innsbruck, Austria

[5]Christian Doppler Laboratory for Iron and Phosphate Biology, Medical University of Innsbruck, Austria

Background

Conventional tumour models inadequately replicate the complex tumour microenvironment, contributing to high failure rates of new drug candidates. To address this gap, we explored normothermic liver machine perfusion (NLMP), a technology initially developed for organ transplantation, as a platform for more physiologically relevant ex-situ tumour research. In this proof-of-concept study, we assessed the feasibility of NLMP as a tumour model and evaluated an adeno-associated virus (AAV) capsid library for targeted gene delivery in hepatocellular carcinoma (HCC) tissue.

Methods

Hepatectomy specimens from HCC patients undergoing liver transplantation were collected, put on ice, flushed with HTK solution, and reconstructed for NLMP. Perfusion was carried out for 24, 36, and 96 hours. Biopsies of HCC and cirrhotic liver tissue were taken and assessed for viability using real-time confocal microscopy (RTCM) and standard histology. Precision-cut liver slices (PCLS) from both tissue types were cultured and infected with a 49-capsid AAV library. DNA was extracted, the AAV transgene was PCR-amplified, and nanopore sequencing was used to quantify capsid-specific barcodes. Capsid preference was analyzed by normalizing barcode counts against the original library input.

Results

All three perfused liver specimens maintained high viability throughout the perfusion period, with RTCM scores ranging from 0 to 1, correlating well with histopathology. In cirrhotic PCLS, AAV distribution was heterogeneous across livers, whereas HCC PCLS exhibited a more consistent pattern. AAV capsid #45 emerged as a dominant variant in all HCC samples, suggesting selective enrichment.

Conclusions

NLMP successfully maintained the viability of both cirrhotic and tumour tissue for up to 96 hours, supporting its potential as a robust tumour model. AAV capsid #45 demonstrated consistent preference for HCC tissue, highlighting its promise for targeted gene therapy in liver cancer.

Unlocking Research Potential: The Use Of Non-Transplanted Human Organs In The Eurotransplant Region

Alexander Kofler[1], Felix J. Krendl[1], Gerald Brandacher[1], Benno Cardini[1], Annemarie Weißenbacher[1], Rupert Oberhuber[1], Stefan Schneeberger[1]

[1]Department of Visceral, Transplant and Thoracic Surgery, Center for Operative Medicine, Medical University of Innsbruck, Austria

Background

Despite the efficiency of the Eurotransplant (ET) network in allocating post-mortem donor organs across eight European countries, a substantial number of organs retrieved for transplantation are ultimately not used. These non-transplanted organs, although unsuitable for clinical use, present significant untapped potential for biomedical research. Current legal and ethical frameworks, however, are often insufficient or ambiguous regarding their secondary use.

Methods

We analyzed ET data from 2014 to 2023 to quantify organs not used for transplantation. Categories included: (i) organs never offered, (ii) offered but not accepted, and (iii) accepted but not transplanted. Yearly totals and subgroup data were assessed for stability using descriptive statistics and by examining deviations from the mean over time. In parallel, we conducted a comparative legal analysis across all ET member states to evaluate national policies on the research use of

non-transplanted organs, with a focus on consent frameworks and regulatory gaps.

Results

Of 100,261 donor organs reported to ET over the 10-year study period, 32.16 % (32,242) were not transplanted. These fell into three categories: never offered (0.74 %), offered but not accepted (15.37 %), and accepted but ultimately not transplanted (16.05 %). The total number of reported organs per year remained stable (mean: 10,026; coefficient of variation: 4.89 %), as did the rates for each non-transplanted subgroup, confirming a consistent and predictable pool of potential research material. National regulations varied: only the Netherlands, Luxembourg, and Slovenia explicitly permit the research use of such organs under defined conditions, while others lack clear provisions.

Conclusions

Non-transplanted but explanted organs represent a stable, ethically accessible resource for biomedical research. Their regulated use could reduce reliance on animal models, maximize donor contributions, and drive medical innovation. Harmonizing legal frameworks across ET countries is essential to unlock this potential and ensure ethical, consistent practice.

Immune Mediator Dynamics Reflect Post-Transplant Immune Remodeling After Alemtuzumab Induction

Oya Berezhinskiy[1], Sophia Auner[1], Shahrooz Nasrollahi Shirazi[1], Sophia Alemanno[1], Clemens Aigner[1], Thomas Wekerle[2], Peter Jaksch[1], Alberto Benazzo[1]

[1]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria
[2]Division of Transplantation, Department of General Surgery, Medical University of Vienna

Background

Calcineurin inhibitor (CNI)-induced nephrotoxicity remains a major limitation in long-term outcomes after lung transplantation (LTx). The ALiKE trial investigates whether CNI exposure can be safely reduced through a combination of low-dose everolimus and tacrolimus following alemtuzumab induction. While alemtuzumab effectively reduces early acute rejection via profound lymphocyte depletion, its long-term immunological effects remain insufficiently characterized.

Methods

Serum samples from 24 ALiKE trial participants (13 receiving alemtuzumab, tacrolimus, and everolimus; 11 receiving alemtuzumab and tacrolimus) were collected at baseline (pre-LTx), and at 6- and 12-months post-transplant. Immune profiling was conducted using the ProcartaPlex™ Human Immune Response 80-Plex panel (Thermo Fisher Scientific) on a Luminex xMAP™ platform. Statistical analyses were performed in R using the Kruskal–Wallis test, followed by Dunn's post hoc test for multiple comparisons.

Results

Several markers showed significant differences both between and within groups. Kruskal-Wallis analysis revealed higher levels of BLC (CXCL13) (p = 0.0088),

Figure 1

GRO alpha (CXCL1)
pretX: p = 0.929 | 6m: p = 0.0284 | 12m: p = 0.104

Granzyme A
pretX: p = 0.285 | 6m: p = 0.443 | 12m: p = 0.942

IL-7
pretX: p = 0.962 | 6m: p = 0.439 | 12m: p = 0.616

IL-34
pretX: p = 0.643 | 6m: p = 0.134 | 12m: p = 0.699

VEGF-A
pretX: p = 0.295 | 6m: p = 0.0124 | 12m: p = 0.0274

MIP-2 alpha (CXCL2)
pretX: p = 0.831 | 6m: p = 0.0253 | 12m: p = 0.38

SCF
pretX: p = 0.289 | 6m: p = 0.831 | 12m: p = 0.487
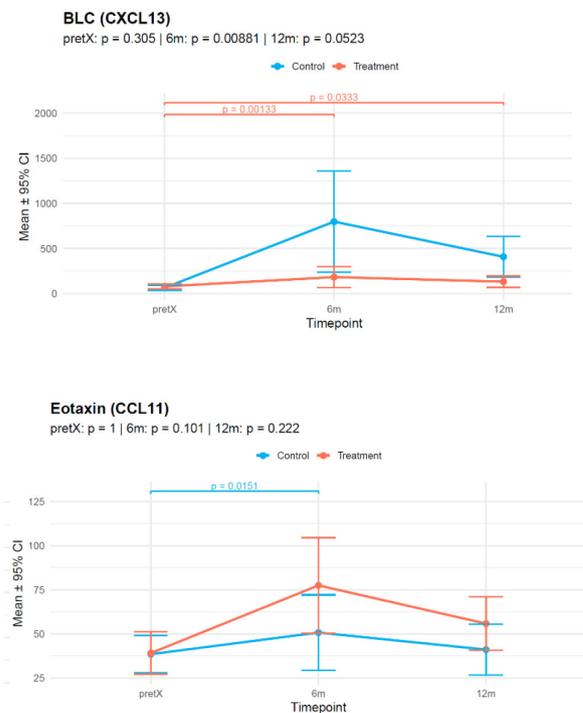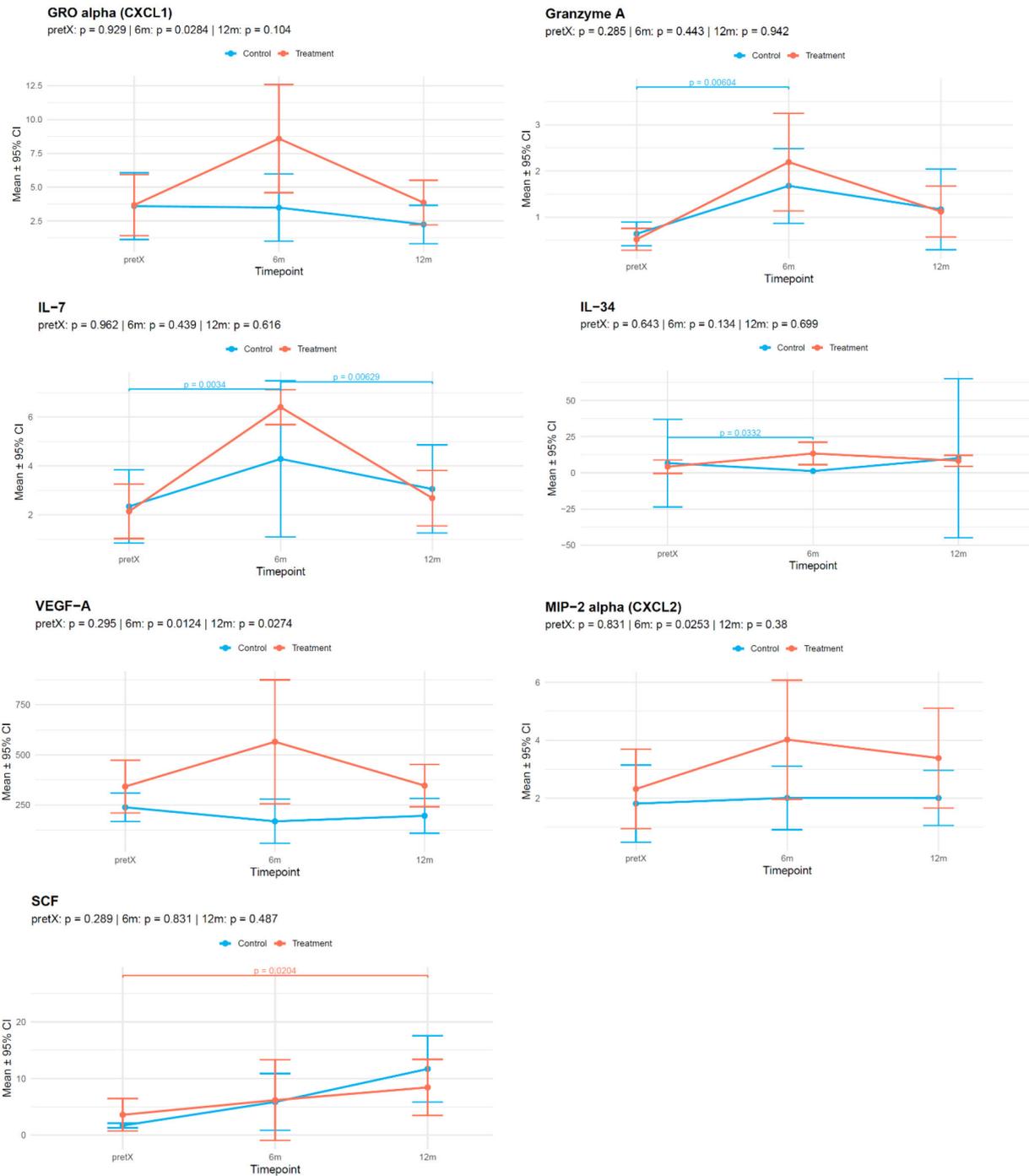
Figure 1

GROα (CXCL1) (p = 0.0284), and MIP-2α (CXCL2) (p = 0.0253) in the treatment group at 6 months, and VEGF-A at both 6 months (p = 0.0124) and 12 months (p = 0.0274).

Within-group comparisons using Dunn's test showed that in the control group, IL-7 increased significantly at 6 months (p = 0.0034) and remained elevated at 12 months (p = 0.0063). Granzyme A (p = 0.0060), IL-34 (p = 0.0332), and Eotaxin (CCL11) (p = 0.0151) also rose from pretx to 6 months. In the treatment group, BLC increased at 6 months (p = 0.0013) and declined by 12 months (p = 0.0333), while SCF rose significantly by 12 months (p = 0.0204).

Conclusion

Alemtuzumab induction was associated with a transient increase in pro-inflammatory, cytotoxic, and angiogenic mediators, peaking at 6 months. These findings suggest an early, time-limited immune activation phase potentially involved in immune reconstitution and tissue repair.

16

Assessment Of Regulatory B Cell Phenotype And IL-10 Expression In Peripheral Blood Of Lung Transplant Patients

Shahrooz Nasrollahi-Shirazi[1], Isabella Grüber[2], Hatice Oya Berezhinskiy[1], Sophia Alemanno[1], Caroline Hillebrand[1], Clemens Aigner[1], and Alberto Benazzo[1]

[1] Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria
[2] University of Veterinary Medicine Vienna, Vienna, Austria

Background

Regulatory B cells (Bregs) are essential for immune tolerance, largely through IL-10 production. However, their phenotypic and functional changes over time, in lung transplant recipients treated with alemtuzumab, remain poorly understood. This study aims to evaluate these changes in Bregs in lung transplant recipients over a one-year period.

Methods

This prospective longitudinal study will include 20 lung transplant recipients treated with alemtuzumab. Blood samples will be collected at three time points: pre-transplantation, 6 months, and 12 months post-transplantation. Whole blood will be stimulated with PMA, ionomycin, and Brefeldin A (PIB), while PBMCs and B cells will be stimulated with CD40L, or CpG, and R848. Breg subpopulations and IL-10 expression will be assessed by flow cytometry. The B cell response to stimuli and functionality, as indicated by cytokine expression, will be analyzed using a human 80-plex kit (which Analyzes 80 cytokine, chemokine, and growth factor targets simultaneously) with Luminex technology.

Results

Preliminary data from two patients at pre-transplantation showed no significant increase in IL-10 expression following stimulation of whole blood. In contrast, healthy donor controls demonstrated approximately a 4-fold increase in IL-10 expression upon stimulation with PIB. However, at pre-transplantation samples, IL-10+ events were enriched in CD24+CD38+ cells. Following PIB stimulation, in addition to CD24+CD38+ cells, an increase in IL-10+ events was observed in CD1d+, CD5+, CD39+, and CD73+ B cells.

Conclusion

This study will offer crucial insights into the phenotypic and functional dynamics of Bregs in lung transplant recipients treated with alemtuzumab. By monitoring changes in Breg phenotype, IL-10 expression, and cytokine expression patterns over time, this research will help better understand Breg-mediated immune tolerance and its potential role in improving transplant outcomes.

Keywords: Regulatory B cells, IL-10, Lung transplantation, Alemtuzumab, Flow cytometry

Allogeneic Stem Cell Transplantation Skews Human Skin TRM Toward Type 1 Polarization At The Expense Of Type 17 Cells

Laura Marie Gail[1, 2], Florian Deckert[1, 3, 2], Luisa Thébault[1], Ruth Dingelmaier-Hovorka[1], Johanna Strobl[1], Lisa Kleissl[2, 1], Denise Eskandari[1], Bärbel Reininger[1], Anna Gabriel[1], Carolina Mayerhofer[1], Christian Freystätter[4], Lisa Ellen Shaw[1], Julia Cserna[3], Lina Zoe Rüsing[3], Wolfgang Weninger[1], Matthias Farlik[1], Werner Rabitsch[3], Georg Stary[1, 2]

[1]Medical University of Vienna, Department of Dermatology, Vienna, Austria
[2]CeMM Research Center for Molecular Medicine, Vienna, Austria
[3]Medical University of Vienna, Department of Medicine I, Vienna, Austria
[4]Medical University of Vienna, Department of Plastic and Reconstructive Surgery, Vienna, Austria

Background

Tissue-resident memory T cells (TRM) are key regulators of skin immunity and inflammation, but their development and functional diversity in humans remain poorly understood. Allogeneic hematopoietic stem cell transplantation (HSCT) offers a unique model to study human TRM biology. After HSCT, host TRM can survive conditioning, while donor T cells infiltrate the skin and establish new TRM. These patients often develop graft-versus-host disease (GVHD), where TRM contribute to tissue damage. These observations raise important questions about how TRM are shaped by the transplant environment and how their altered phenotypes contribute to GVHD. Here, we set out to investigate TRM dynamics in HSCT and GVHD to better understand their contribution to GVHD pathogenesis.

Methods

To explore TRM heterogeneity and turnover after HSCT, we collected serial skin and blood samples from patients post-transplant. We performed single-cell RNA and TCR sequencing, using single nucleotide polymorphisms to distinguish host from donor T cells and track clonal and transcriptional dynamics over time.

Results

We found that the skin TRM pool after HSCT is strongly skewed toward type 1 polarization, with increased IFN-γ expression in TRM. This phenotype is further enhanced during GVHD. In contrast, type 17–polarized TRM are significantly reduced after HSCT and during GVHD, recovering only months later. These changes suggest that the transplant conditioning and post-transplant immune environment promote type 1 TRM development while suppressing type 17 lineages.

Conclusions

HSCT induces a long-lasting imbalance in the skin TRM compartment, favoring type 1– over type 17–polarized cells. This skewing is exacerbated during GVHD and may contribute to disease pathogenesis. Early activation and polarization phenotypes of TRM may be explored as biomarkers for GVHD susceptibility in the future. Understanding the environmental and molecular cues driving this polarization could reveal novel strategies for targeting TRM in inflammatory skin diseases and transplant-related complications.

From Bedside To Bench And Back: The "Innsbruck Model" For Reduction And Refinement In Large-Animal Organ Perfusion

Simon Mathis[1], Thomas Resch[2], Florian Ponholzer[2], Gabriel Putzer[1], Christina Bogensperger[2], Franka Messner[2], Julia Hofmann[2], Anne Heberle[2], Marlene Pühringer[2], Theresa Hautz[2], Stefan Schneeberger[2], Gerald Brandacher[2], Judith Martini[1]

[1] Department of Anesthesia and Intensive Care Medicine, Medical University of Innsbruck, Austria
[2] OrganLife Laboratory and Daniel Swarovski Research Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Center of Operative Medicine, Medical University of Innsbruck, Austria

Background

While replacement of animal experiments remains a major objective in biomedical research, large-animal models continue to be indispensable in the field of experimental ex vivo organ perfusion. In this abstract, we present the "Innsbruck Model" as a structured approach to reduce and refine animal experimentation in accordance with the 3R principles.

Methods

In this model, domestic pig organs are utilized for multiple simultaneous research purposes. Following anesthesia of the pig using human clinical standards, including intubation and ultrasound-guided femoral vessel cannulation for blood pressure monitoring, the animal undergoes controlled hemorrhage to collect autologous blood. This blood is then used to perfuse the simultaneously explanted liver, kidneys, and lungs. The skin is preserved for dermatological studies, and the pancreas is harvested for tissue research, replacing the need for approximately 50 murine pancreata.

Following organ harvesting, post-mortem educational use includes surgical training, such as bowel anastomosis suturing, performed by clinical trainees.

Results

While the comprehensive use of multiple organs and tissues from a single animal presents considerable logistical and physiological challenges, it becomes feasible through a structured interdisciplinary collaboration between anesthesiologists, transplant surgeons and intensive care physicians to deliberately transfer clinical expertise back into experimental research. By enabling translational procedures under near-clinical conditions, the model enhances physiological relevance, clinical applicability and validity of collected data while simultaneously reducing overall animal numbers.

Conclusion

Through close collaboration between disciplines, human intensive care principles are applied to the animal model. This enables optimized experimental conditions, allowing multiple high-quality experiments to be conducted from a single animal.

The "Innsbruck Model" demonstrates that translational research is bidirectional: integrating clinical standards into preclinical animal studies elevates scientific rigor and reduces animal use. Clinical expertise contributes substantial experience and precision, enhancing the quality and reproducibility of organ perfusion experiments while establishing an ethical research framework.

03_Heart Transplantation

19

Personalized Risk Stratification After Heart Transplantation: Prognostic Role Of Alkaline Phosphatase Drop And Plasma Volume Status

Kira Osipenko[1], Thomas Poschner[1], Alexandra Kaider[2], Luca Conci[1], Thomas Putz[1], Rabab Saleh[1], Amila Kahrovic[1], Martin Andreas[1], Daniel Zimpfer[1], Markus Mach[1], Dominik Wiedemann[1], Andreas Zuckermann[1], Emilio Osorio[1]*

[1] Department of Cardiac and Thoracic Aortic Surgery, Medical University Vienna, Austria
[2] Center for Medical Data Science, Institute of Clinical Biometrics, Medical University Vienna, Austria

Background

Risk stratification after heart transplantation (HTX) remains challenging. Existing scores rely mostly on static preoperative variables and fail to reflect dynamic physiological responses. We aimed to investigate

the prognostic value of early postoperative alkaline phosphatase (AP) drop and plasma volume score (PVS) as dynamic, accessible markers after HTX.

Methods

We conducted a retrospective single-center study including 375 adult HTX patients (2012–2023). The percentage AP drop on postoperative day 1 (POD1) and preoperative PVS were assessed. One-year and 30-day outcomes were analyzed using Cox and logistic regression. Non-linear effects of AP drop and AP ratio at POD6 were modeled using quadratic and log-transformed terms, respectively.

Results

A greater AP drop was strongly associated with increased mortality. At a POD1 AP drop of 62%, each 5-unit increase raised 1-year mortality risk by 28% (adjusted HR = 1.27, $p < 0.001$). Patients with AP drop $\geq 61.54\%$ had lower 1-year survival (78.5% vs. 92.2%, $p = 0.0002$) and higher 30-day mortality (OR = 3.82, $p = 0.030$). Higher AP drop was also linked to dialysis requirement (OR = 3.66, $p < 0.0001$). On POD6, lower AP ratios (log2-transformed) were significantly associated with improved survival ($p = 0.0002$). PVS ≥ 3.1 independently predicted 1-year mortality (adjusted HR = 2.11, $p = 0.0235$) and dialysis requirement (OR = 1.14 per 5-unit increase, $p = 0.0439$).

Conclusions

Early postoperative AP drop and preoperative PVS are strong, dynamic, and independent predictors of mortality and organ dysfunction after HTX. Their integration into risk models may improve early stratification and support personalized postoperative care.

Extracorporeal Photopheresis And Reduced-Intensity Immunosuppression In High-Risk Heart Transplant Recipients: A Retrospective Cohort Study

Alissa Florian [1], Keziban Uyanik-Ünal [1], Hümeyra Erdogan [1], Luca Conci [1], Emilio Osorio [1], Alexandra Kaider [2], Daniel Zimpfer [1], Arezu Aliabadi-Zuckermann [1], Andreas Zuckermann [1], Nina Worel [3]

[1] Department of Cardiac and Thoracic Aortic Surgery, Medical University Vienna, Vienna, Austria
[2] Institute of Clinical Biometrics, Center for Medical Data Science, Medical University of Vienna, Austria
[3] Department of Transfusion Medicine and Cell Therapy, Medical University Vienna, Vienna, Austria

Background

High-risk heart transplant (HTx) recipients, including those with prior malignancy, perioperative temporary mechanical circulatory support (tMCS), or active infections, present major challenges to conventional immunosuppressive strategies. We evaluated our approach combining extracorporeal photopheresis (ECP) with reduced-intensity immunosuppression in this complex population.

Methods

In this retrospective single-center analysis, 65 adult HTx recipients (2016-2024) were treated according to our reduced-intensity immunosuppressive protocol. Patients were stratified by primary indication: prior malignancy (n=12), tMCS (n=22), and active infection (n=31). All patients received standardized immunosuppression with delayed tacrolimus, mycophenolate and low-dose corticosteroids, alongside 12 ECP cycles over 6 months. Primary outcome was overall survival;

secondary outcomes included rejection, renal function, development of donor-specific antibodies (DSAs), and infectious complications.

Results
Median follow-up was 28.8 months. One-year survival was 83.97% overall and 100% in the malignancy group, 80.4% in the tMCS group and 80.2% in the infection group, without any intergroup differences (p=0.998). Renal function remained stable across the follow-up timepoints. 15.6% of patients developed DSAs within the first year after HTx, overall DSA development was 31.98% in Kaplan-Meier analyses with death as a competing event. Acute cellular rejection ≥2R (ISHLT classification) within the first year after HTx occurred in 16.9% of patients, with no antibody-mediated rejection (AMR) ≥2. ICU and hospital stays, as well as infetion rates were comparable across subgroups.

Conclusions
ECP-based reduced-intensity immunosuppression is feasible and safe in high-risk HTx recipients, offering promising survival and renal outcomes without compromising immune control. This strategy may facilitate personalized immunosuppression, decoupling traditional risk factors from adverse outcomes through targeted immune modulation.

21

Donation After Circulatory Determination Of Death Heart Transplantation – Early Experiences From Innsbruck

Lukas Stastny[1], Michael Graber[1], Leo Pölzl[1], Felix Nägele[1], Nikolaos Bonaros[1], Gerhard Pölzl[2], Robert Breitkopf[3], Nikolaos Bonaros[1], Michael Grimm[1], Stephan Eschertzhuber[4], Julia Dumfarth[1]

[1]Department of Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Internal Medicine III, Cardiology & Angiology, Medical University of Innsbruck, Innsbruck, Austria
[3]Department of Anaesthesiology and Critical Care Medicine, Medical University of Innsbruck, Innsbruck, Austria
[4]Department of Anesthesia and Intensive Care Medicine, Hospital Hall, Hall, Austria

Background
Donation after circulatory determination of death (DCD) is an emerging strategy to expand the donor heart pool. We describe our center's initial experience with DCD heart procurement using direct procurement and ex-situ machine perfusion in Innsbruck.

Methods
From February 2023 to June 2025, eight DCD hearts were procured using direct procurement followed by ex-situ machine perfusion with the Organ Care System (OCS). One heart was deemed unsuitable for transplantation. Seven DCD hearts were transplanted into recipients selected according to standard criteria. Donor characteristics and recipient outcomes were collected.

Results
A total of seven DCD heart transplants were performed. Donors had a median age of 29 years (range 15–34), with four male and three female donors. Median functional warm ischemia time was 26 minutes (IQR 24–28), and median ex-situ perfusion time was 230 minutes (IQR 200–300). Recipients ranged from 15 to 65 years (median 57), with indications including dilated cardiomyopathy (n = 4), ischemic cardiomyopathy (n = 2), and arrhythmogenic right ventricular cardiomyopathy (n = 1). All recipients survived to discharge; no cases of primary graft dysfunction occurred. Median ICU stay was 4 days (range 3–6).

Conclusion
Our initial experience demonstrates that DCD heart transplantation using direct procurement and ex-situ perfusion is feasible and safe in a newly established program. These promising outcomes support further development of DCD protocols to increase donor heart availability in Austria.

04_Kidney Transplantation

Case Report: Delayed Graft Function And Therapy-Resistant Arterial Hypertension Following Kidney Transplantation Due To Kinking Of The Transplant Artery – A Rare Occurrence?

Lorenz Kircher, Michael Sereinigg, Konstantin Klötzer, Robert Sucher, Phillip Stiegler

Department for general-, visceral- and transplant surgery, Medical University of Graz, Graz, Austria

Background

We report on a 60-year-old male patient of ethnic descent, who was referred to our transplant centre for his first kidney transplant. The patient has been suffering from dialysis-dependent chronic kidney disease (CKD G5A3) for three years due to malignant arterial hypertension. After allocation, the patient underwent an uneventful kidney transplant in the right iliac fossa at our centre. Despite an initially unremarkable direct postoperative course with normal NTX sonography, the patient developed a severe and therapy-resistant hypertensive episode and delayed graft function (DGF).

Methods

Initial sonography of the transplant kidney revealed slightly reduced perfusion in the caudal pole, but the renal arterial resistive index (RI) was unremarkable at around 0.7, indicating normal arterial blood flow. Despite maximal antihypertensive therapy (six medications), including a Clevidipine perfusor, normotensive blood pressure could not be achieved. On the fourth postoperative day (POD), a post-stenotic flow profile was first described in the daily sonography control, and a CT angiography was performed. This confirmed kinking of the transplant artery, and a decision for surgical revision was made.

Results

Intraoperatively the anastomoses were initially unremarkable and the kidney was homogenously perfused, but kinking of the transplant artery was noted. After repositioning and flow measurements, a normal flow profile and excellent perfusion were restored. Immediately after repositioning, the patient's hemodynamic status improved, and normotension was achieved on the following day. Serum creatinine decreased immediately postoperatively, diuresis improved and sonography showed improved flow measurements. Three days later the patient was transferred to the nephrology ward with good diuresis, regressed renal retention parameters and normotension. He was discharged 18 days after the transplant.

Conclusions

In cases of therapy-resistant hypertension and DGF after kidney transplantation, even with initially unremarkable sonography, kinking of the renal artery due to changes in the transplant's position should be considered and prompt surgical revision should be performed.

Management Of Lymphoceles After Kidney Transplantation: Two Years Follow-Up

Nadina Roth, Manfred Kalteis, Axel Krause, Klaus Krichbaumer, Jürgen Huber, Matthias Biebl

Department of Surgery, Ordensklinikum Elisabethinen Linz, Austria

Background

Lymphoceles are a surgical complication after transplantation and range worldwide between 0.5-16%. We present long-term results of percutaneous drainages, sclerosis in lymphnodes and laparoscopic lymphocele fenestration.

Methods

We retrospectively reviewed 120 kidney transplantations from November 2022 to November 2024. 7 (5.8%) presented a complicated lymphocele after transplantation. After CT scan and pigtail treatment without success catheters were positioned under ultrasound guidance. Then sclerotherapy with Lipiodol Glubran 4:1 was applied, in three times a second application two days later was necessary. Finally two lymphocele fenestrations had to be done to stop the serome.

Results

The management with Lipiodol-Glubran 4:1, when lymphoceles are detected, is very sufficient. Mean initial size of lymphoceles was a mean initial volume of 11x5x8cm

The mean duration of CT scan with pig tail drainage , lymphnode sclerotherapy and operation was 19 days The average volume in one sitting was 7 ml. No recurrrence or graft loss was seen, no late complication occured.

Conclusions

Drainages and US guided catheters with Lipiodol-Glubran 4:1 sclerosis is a safe treatment of symptomatic lymphoceles, it´s also cost effective. Laparoscopic fenestration can be used in case of failure.

Retrospective Assessment Of Vascular Anatomy Visualization Via 3D Reconstruction In Robotic-Assisted Living Donor Nephrectomy

Mohamed El-Mahrouk, Beatrice Lukenaite, Robert Sucher, Saulius Mikalauskas

Division of General, Visceral and Transplantation Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

Background

Patient safety is paramount in donor nephrectomy. Recently, individualized 3D reconstructions from cross-sectional imaging have gained traction to optimize preoperative planning. This study evaluates whether such reconstructions based on CT imaging improve anatomical assessment and surgical preparation in robotic donor nephrectomy.

Methods

This retrospective single-center study included 24 patients who underwent robotic donor nephrectomy between 2022 and 2025. Patient-specific 3D models were created using MED EINS software and compared with conventional CT reports for vascular anatomy assessment.

Results

Of the 24 completed nephrectomies, 75% were left-sided. No intraoperative complications occurred; minor postoperative complications were observed in 16.7% of cases. Donors had a mean age of 52.9 years and a mean BMI of 28.0. Most had a single renal artery (83.3%) and vein (91.7%). The average operative time was 205 minutes, and the mean hospital stay was 6.4 days. Donor-recipient relationships included children and partners (41.7% each), followed by friends (8.3%) and cousins or siblings (4.2% each).

3D reconstructions showed high concordance with standard CT reports. In one case, a second artery missed in the CT report was identified intraoperatively but could be retrospectively visualized clearly in the 3D model, highlighting its potential value in detecting anatomical variants.

Conclusion
Individualized 3D reconstructions can support and refine preoperative planning in robotic donor nephrectomy by enhancing anatomical visualization. However, their clinical benefit should be further validated in prospective studies.

25

Body Mass Index: A Key Factor In Surgical Site Infections After Kidney Transplantation?

Mohamed El-Mahrouk[1], Raphaela Sorgnitt[1], Schwantzer Gerold[2], Derar Jaradat[1], Zoltan Mathe[1], Robert Sucher[1], Daniela Kniepeiss[1]

[1] Division of General, Visceral and Transplantation Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
[2] Medical informatics, statistics and documentation, Medical University of Graz, Graz, Austria

Background
Kidney transplant recipients are highly susceptible to surgical site infections (SSIs) due to the procedure's complexity and immunosuppression. This study examines the impact of BMI on SSI risk and identifies common causative microorganisms.

Methods
This single-center study was conducted as a retrospective analysis of 230 renal transplant patients between 2017 and 2019. The standard antibiotic administered was a cephalosporin. All patients who developed a SSIs underwent a wound swab.

Results
SSIs occurred in 45 patients (19.6%) and showed no significant association with age (p = 0.744), sex (p = 0.605), or donor type (p = 0.277). The most frequently isolated organisms were coagulase-negative staphylococci (26.7%), Staphylococcus epidermidis (24.5%), Enterococcus faecalis (22.2%), and Candida albicans (22.2%). SSIs were significantly associated with the need for surgical revision (p < 0.001) and a higher BMI (p = 0.027). Patients with a BMI $\geq$ 28.1 had a threefold increased risk of developing an SSI (OR = 3.0; p = 0.001). Notably, each one-unit increase in BMI was linked to a 7.2% rise in the odds of SSI (OR = 1.072; 95% CI: 1.011–1.138; p = 0.020). Similarly, patients with a BMI $\geq$ 28.1 had a significantly higher risk of SSIs compared to those with a BMI < 28.1 (OR = 3.0; 95% CI: 1.6–5.9; p = 0.001). Additionally, individuals with a BMI > 28,1 had a significantly higher incidence of infections caused by Staphylococcus (p = 0.019) and Enterococcus (p = 0.048).

Conclusion
Surgical site infections are a frequent early complication after kidney transplantation, contributing to morbidity. Standard antimicrobial regimens may miss key pathogens, especially in patients with high BMI. Future studies should optimize prophylaxis for high-risk groups.

26

Intragraft Interferon-Stimulated Gene Expression Is Associated With Viral Clearance In BK Polyomavirus-Associated Nephropathy

Haris Omic[1] Md, Nicolas Kozakowski[2] Md, Johannes Kläger[2] Md, Daniela Gerges[1] Md Phd, Zeljko Kikic[3], Michael Eder[1] Md

[1.] Division Of Nephrology And Dialysis, Department Of Medicine Iii, Medical University Of Vienna, Vienna, Austria
[2.] Department Of Pathology, Medical University Of Vienna, Vienna, Austria
[3.] Department Of Urology, Medical University Of Vienna, Vienna, Austria

Prediction Of Antibody-Mediated Rejection By Quantifying Eplets Potentially Targeted By Preformed Donor-Specific Antibodies

Konstantin Doberer[1], Sebastian Kapps[1], Daniela Kriks[2], Gottfried Fischer[2], Luis G. Hidalgo[3], Farsad Eskandary[1]

[1] Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[2] Department of Transfusion Medicine and Cell Therapy, Medical University of Vienna, Vienna, Austria
[3] Department of Surgery, University of Wisconsin, Madison, Wisconsin, USA

Background

Due to missing effective antiviral treatments, BK polyomavirus-associated nephropathy (BKPyVAN) remains a threat to graft function and survival after kidney transplantation. Effective management of BKPyVAN is challenging, due to the required fine balance between antiviral responses and graft rejection. Furthermore, risk factors for treatment failure are unknown. This study aims to identify beneficial intragraft gene expression patterns associated with viral clearance in kidney transplant recipients with definite BKPyVAN.

Methods

In this retrospective analysis, the first of its kind in BKPyVAN, we analyzed gene expression profiles in biopsy samples from 30 kidney transplant recipients diagnosed with definite BKPyVAN, utilizing the NanoString nCounter system. Our primary hypothesis was to identify gene expression patterns associated with clinical outcomes, specifically viral load clearance 6- and 12 months after BKPyVAN diagnosis.

Results

In patients with viral clearance six months post-diagnosis, ISG15, IFI27, and IFIT1 were notably upregulated with log fold changes (logFC) of 1.84, 1.46, and 1.62, respectively (adjusted p-values: 0.0059 for ISG15, and 0.0083 for both IFI27 and IFIT1). IFITM1 also showed significant upregulation with a logFC of 1.41 (adjusted p-value 0.015). In patients with viral clearance 12 months after diagnosis, IFI27 exhibited the most substantial upregulation with a logFC of 1.73 (adjusted p-value 0.00007). ISG15 and IFIT1 were also upregulated with logFC values over 1.86 and 1.87, respectively (adjusted p-values 0.00012).

Discussion

Our analysis identified significant upregulation of interferon-associated genes in patients achieving viral clearance. Their expression inversely correlates with viral load over time, highlighting their potential regulatory roles in viral clearance. Similar to previous studies from patients with COVID and RSV, our findings suggest that in renal transplants, interferon-inducible genes are involved in anti-viral immune response. We hypothesize that intragraft gene expression monitoring could help identify patients with insufficient immune responses and risk of subsequent treatment failure.

Background

Preformed donor-specific antibodies (DSA) may cause antibody-mediated rejection (ABMR) despite potent desensitization protocols. Mean fluorescence intensity (MFI) serves as surrogate for DSA "strength" and associates with antibody-mediated rejection (ABMR). HLA molecular mismatch studies have mostly focused on the formation of *de novo* DSA. However, the potential for molecular mismatch calculations to aid in post-transplant risk stratification for preformed DSA remains unexplored.

Methods

This retrospective study evaluated deceased-donor kidney transplant (KTX) recipients who underwent peri-transplant desensitization for preformed DSA between 2012 and 2020. A specific eplet mismatch score was calculated for each donor-recipient-pair via restriction to eplets targeted by the specific DSA(s). Four-digit HLA typing was mandatory for inclusion. The primary outcome was biopsy-proven ABMR according to the Banff 2022 classification.

Results

63 patients had available data for inclusion: 32 were female (51%) and 43 (68%) had received an earlier KTX. Median HLA (A/B/DR) mismatch was three (IQR 2-4). Patients had a median number of two DSA (IQR 1-3) and median follow-up

was 5.2 years. Twenty-three individuals showed ABMR (37%), at median of 1.3 years (IQR 0.1-3.8). Overall eplet mismatch was not different between the groups (64 [IQR 41-76] vs 56 [IQR 32-66]; *p=0.186*). However, when the eplet analysis was restricted to the specific HLA targets of the preformed DSA(s), patients who subsequently showed ABMR had a significantly higher score compared to those without ABMR (21 [IQR 14-27] vs 11 [6-19]; *p=0.002*). Notably, in a multivariable logistic regression model DSA eplet mismatch score predicted ABMR after correction for MFI max (AUC 0.74; OR 1.08, 95% [CI 1.01, 1.15]).

Conclusion

Our data suggests that DSA-restricted eplet mismatch scores predict ABMR. This implies that the number of epitope targets for pre-existing DSA contributes to the degree of DSA-mediated damage and translates into histologic ABMR. Larger cohorts are needed to validate this finding.

28

Main Statistical Aspects Of The TTVguideIT Trial – A Randomized Controlled Trial Investigating Biomarker-Guided Immunosuppression In Kidney Transplant Recipients

Felix Herkner[1,2], Frederik Haupenthal[1], Sebastian Kapps[1], Konstantin Doberer[1], Harald Herkner[3], Franz König[2,*], Gregor Bond[1,*]

[1] Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[2] Center for Medical Data Science, Medical University of Vienna, Vienna, Austria
[3] Department of Emergency Medicine, Medical University of Vienna, Vienna, Austria
*Both authors share last authorship

Background

Preliminary studies show an association of Torque-Teno-Virus (TTV) blood load and outcomes in kidney transplant populations. This makes it an auspicious candidate for biomarker-guided immunosuppression after transplantation. The TTVguideIT trial aims at investigating the safety, tolerability and preliminary efficacy of TTV-guided immunosuppression.

Choices of design, statistical analysis methods, and reporting, among others, can influence results and conclusion drawn from clinical trials. According to the ICH E9 guidelines, statistical analysis should be preplanned and described in advance in the protocol and possibly in an additional statistical analysis plan (SAP) providing more details on the methods and reporting.

Methods

Here we present the SAP for the TTVguideIT trial, a randomised, controlled, interventional, two-arm, non-inferiority, patient- and assessor-blinded, international multicentre and investigator-driven phase II trial. A total of 260 stable, low-immunological-risk adult kidney transplant recipients with TTV infection receiving Tacrolimus-based immunosuppression are recruited three months post-transplant in 13 academic centres in six European countries. Subjects are randomised at a 1:1 allocation ratio stratified by centre to receive Tacrolimus guided by TTV load or according to the local centre standard of care for nine months. The primary composite endpoint combines infections, biopsy-proven allograft rejection, graft loss and death. Secondary outcomes are among others protocol biopsy at month twelve post-transplant, development of *de novo* donor-specific antibodies, health-related quality of life and drug adherence measurements.

Results and Conclusion

Key aspects of the design and the main analysis strategies are presented. The sample size calculation incorporates both aspects of testing non-inferiority and superiority for the TTVguideIT trial. This is enabled by testing non-inferiority followed by hierarchical testing of superiority of the binary primary composite endpoint covering the aforementioned endpoints. To facilitate a proper interpretation, further analyses are presented for secondary endpoints including supportive and sensitivity analyses. Both planned analyses and reporting will be presented and discussed.

References and links

Haupenthal, F., Rahn, J., Maggi, F. et al. A multicentre, patient- and assessor-blinded, non-inferiority, randomised and controlled

phase II trial to compare standard and torque teno virus-guided immunosuppression in kidney transplant recipients in the first year after transplantation: TTVguideIT. Trials 24, 213 (2023). https://doi.org/10.1186/s13063-023-07216-0

European Medicines Agency (EMA). ICH Topic E 9: Statistical principles for clinical trials (1998). CPMP/ICH/363/96. Available at https://www.ema.europa.eu/en/ich-e9-statistical-principles-clinical-trials-scientific-guideline. (Online; accessed 23 June 2025.)

29

Comparing The Statistical Power Of Methods For The Analysis Of Multiple Endpoints In Kidney Transplant Trials

Felix Herkner[1,2], Martin Posch[1], Gregor Bond[2], Franz König[1]

[1] Center for Medical Data Science, Medical University of Vienna, Vienna, Austria
[2] Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria

Background

The infeasibility of sample sizes needed for making decisions based on traditional primary endpoints like patient or graft survival is a common issue in kidney transplant trials. A potential solution is to consider more than one endpoint in the primary analysis. Options to handle several endpoints for the primary analysis, as discussed in the FDA and EMA guidance documents on the use of multiple endpoints in clinical trials, include the use of composite endpoints defined as the first of any of the single outcomes to occur. Alternatively, testing of single components and applying multiplicity correction can be performed, e.g., embedded in a tailored closed testing strategy using weighted tests. The aim of this simulation study is to assess the impact of different endpoint types and corresponding analysis strategies (e.g., based on a binary or a time-to-event scale) on statistical power.

Methods

Simulations of patient-level data in settings motivated by a randomized controlled multi-center study investigating a novel biomarker for guiding immunosuppression - the TTVguideIT trial - are performed to estimate the power of the aforementioned approaches. Different assumptions regarding the distributions of the individual components of the composite endpoint are investigated.

Results

Although there is no single most powerful method across all scenarios, composite endpoint strategies proved to be more powerful than testing individual endpoints in the majority of considered scenarios. Weighted tests can selectively enhance power in certain scenarios. Transformation of the composite time-to-event endpoint to a binary composite endpoint seems to be feasible with marginal power loss.

Conclusion

We discuss the advantages and disadvantages of different strategies regarding their power, practical application and interpretation of the treatment effect to facilitate the choice of endpoints and analysis strategies in kidney transplant trials.

References and links

Haupenthal, F., Rahn, J., Maggi, F. et al. A multicentre, patient- and assessor-blinded, non-inferiority, randomised and controlled phase II trial to compare standard and torque teno virus-guided immunosuppression in kidney transplant recipients in the first year after transplantation: TTVguideIT. Trials 24, 213 (2023). https://doi.org/10.1186/s13063-023-07216-0

U.S. Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Multiple Endpoints in Clinical Trials. Guidance for Industry. (2022). Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/multiple-endpoints-clinical-trials. (Online; accessed 23 June 2025).

European Medicines Agency (EMA), Committee for Proprietary Medicinal Products (CPMP). Points to consider on multiplicity issues in clinical trials. (2002). Available at https://www.ema.europa.eu/en/documents/scientific-guideline/points-consider-multiplicity-issues-clinical-trials_en.pdf. (Online; accessed 23 June 2025).

Living Kidney Donation Of Kidney With Renal Artery Aneurysm

Emerson L. Monteiro[1], Mohamed El-Mahrouk[1], Helmut Müller[2], Daniela Kniepeiss[1]

[1]Department of general, visceral and transplantation Surgery, Medical University of Graz, Graz, Austria
[2]Department of vascular Surgery, Medical University of Graz, Graz, Austria

Background
Renal artery aneurysm (RAA) is a rare condition characterized by a localized dilation of the renal artery, often discovered incidentally during imaging for unrelated reasons. Symptoms vary from none to secondary hypertension or, in rare cases, rupture—typically depending on the aneurysm's size. This case report describes the incidental discovery of an RAA in a living kidney donor during routine evaluation and preparation for donation.

Case Presentation
During the preoperative assessment of a living kidney donation for a recipient with end-stage renal disease due to Hinman syndrom, a 7 mm asymptomatic saccular RAA was unilaterally detected at the donor. The affected kidney was deliberately selected for donation to enable a preemptive ex vivo aneurysm repair, thereby minimizing future risks to both the donor and recipient. Following donor nephrectomy, the aneurysm was repaired on the back table via clipping before transplantation. After 2:20 hour surgery the intraoperative flow measurements and postoperative Doppler ultrasound confirmed good perfusion. No early complications were observed, the Kreatinin level of the recipient dropped immediately after surgery from 3,6 mg/dL to 1,36mg/dL and both donor and recipient were discharged without delay, with good postoperative kidney function.

Discussion
When RAA is detected in a living kidney donor, selecting the affected kidney for donation—combined with ex vivo aneurysm repair—can be beneficial for both parties. The recipient receives a timely, immunologically compatible transplant without prolonged waiting. Meanwhile, the donor is relieved of the long-term risks associated with untreated RAA, including rupture, hematuria, or secondary hypertension, as well as the need for regular follow-up imaging.

Conclusion
Growing evidence from case reports, including this one, supports the safety and feasibility of living kidney donation from donors with RAA following ex vivo vascular repair.

De Novo Longterm-Release Tacrolimus Enhances T Cell Suppression In Patients With Low Concentration-To-Dose Ratios After Kidney Transplantation — A Matched Cohort Analysis

Simon Aberger[1,2], Max Schuller[1], Agnes A Mooslechner[1,3], Konstantin A Klötzer[1], Barbara Prietl[4,5], Verena Pfeifer[4,5], Alexander H Kirsch[1], Alexander R Rosenkranz[1], Katharina Artinger[1], Kathrin Eller[1]

[1]Division of Nephrology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2]Department of Internal Medicine I, Nephrology, Paracelsus Medical University, Salzburg, Austria
[3]Otto Loewi Research Center, Division of Pharmacology, Medical University of Graz, Graz, Austria
[4]Center for Biomarker Research in Medicine, Graz, Austria
[5]Division of Endocrinology and Diabetology, Department of Internal Medicine, Medical University of Graz, Graz, Austria

Background
A low concentration-to-dose (C/D)-ratio is known to identify patients at higher risk of allograft rejection as early as 2 months after kidney transplantation (KT). Understanding how different tacrolimus formulations

influence T cell activation over time in relation to the C/D-ratio may allow to optimize tacrolimus prescription.

Methods
T cell activation profiles were compared between 30 patients started on de novo longterm-release tacrolimus (LCPT) and 30 propensity score matched patients started on immediate-release tacrolimus (IRT). T cell phenotyping by flow cytometry along with assessment of clinical data were performed before KT and during study visits 10 days, 2 months and 12 months after KT.

Results
Longitudinal T cell phenotyping revealed a stronger suppression of T cell activation markers (HLA-DR, CD147, FCRL3) with LCPT throughout the observational period. Overall tacrolimus exposure was higher with LCPT. A 63% reduction in activation-proliferation marker HLA-DR in CD4+ T cells reflected an 18% increase in tacrolimus exposure among patients with low C/D-ratios at month 2, otherwise known to experience low trough levels with inherent risk of rejection.

Conclusions
De novo LCPT improved tacrolimus exposure and enhanced T cell suppression in patients with low C/D-ratios determined 2 months after KT.

32

Robotic-Assisted Kidney Transplantation – Update From Vienna

Jakob Eichelter[1], Jeannette Widmer[1], Julia Jedamzik[1], Georg Györi[1], Andreas Salat[1], Gabriela Berlakovich[1]

[1]Division of Transplantation Surgery, Department of General Surgery, Medical University of Vienna, Vienna, Austria

Background
While minimally-invasive surgery is considered state of the art in most surgical fields, it is still an emerging technique in transplantation surgery due to its technical and organizational challenges. Robotic-assisted kidney transplantation (RAKT) has shown positive outcomes compared to open surgery. Meta analyses conclude comparable functional outcomes, but shorter incision length, favorable postoperative pain and reduced risk for postoperative complications. Especially common complications like lymphoceles and surgical site infections almost vanished, which is a major advantage in increasing obesity in recipients.

Methods
After training of the surgical team and with guidance by a proctor, RAKT was established in November 2024 using the Da Vinci Xi ® system (Intuitive Surgical, Inc., 1020 Kifer Road, Sunnyvale, CA 94086). All patients and organs for scheduled transplantations (living donations) were evaluated for robotic transplantation.

Results
Between 11/2024 and 06/2025 eighteen kidney transplantations through living donations were performed. Thirteen patients received a RAKT, five patients open transplantation due to the following reasons: atherosclerosis, short ureter (2 pat.), patient´s choice for open surgery and technical reasons. No intraoperative complications occurred; no conversion was necessary.

Conclusions
RAKT is a complex procedure but promises beneficial results for kidney transplant recipients, especially by tackling high complication rates in obese patients with open surgery.

33

Microdialysis During Normothermic Machine Perfusion Of The Kidney

Katharina Joost[1], **Michael Dullnig**[1], Simon Mathis[1], Thomas Resch[2], Gabriel Putzer[1], Franka Messner[2], Marlene Pühringer[2], Theresa Hautz[2], Judith Martini[1]

[1]Department of Anaesthesiology and Critical Care Medicine, Medical University of Innsbruck, Innsbruck, Austria

[2]organLife Organ Regeneration Center of Excellence, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background

Although normothermic machine perfusion is a promising technique for kidney transplantation, the metabolic assessment of this heterogeneously structured organ remains challenging.[1] Microdialysis (MD) enables real-time monitoring of extracellular metabolism and has been previously applied in kidneys preserved by static cold storage (SCS) and hypothermic machine perfusion.[2] Here we present the first data on the use of microdialysis during kidney NMP.

Methods

Five porcine kidneys were explanted and initially stored under SCS conditions. During SCS, a microdialysis catheter was implanted into the renal cortex. The baseline measurement was taken under SCS, followed by 24 hours of NMP. In the initial perfusion period, microdialysate samples were collected at 30-minute intervals, followed by hourly collections. Lactate and pyruvate concentrations were measured using an ISCUSflex analyzer, allowing calculation of the lactate-to-pyruvate (L/P) ratio.

Results

MD was technically feasible over the full 24-hour NMP period without complications. Pyruvate concentrations in the microdialysate showed very low values during SCS (0.84 µM (IQR 0.43−1.35)), with a rapid increase after start of NMP and a stabilization around 100−150 µM. Lactate concentrations showed a typical course: After an initial peak (4.64 mM (IQR 4.57−4.71)) 30 minutes after the start of NMP, the levels fell and stabilised before rising again towards the end of perfusion. The L/P ratio was markedly elevated under SCS (1976.56 (IQR 1150.49−3498.96)), reflecting anaerobic metabolism, and dropped sharply after initiation of NMP. L/P ratio stabilized around values of 10−20, with a mild upward trend after 20 hours of NMP.

Conclusion

MD proved technically feasible and stable during 24-hour NMP in porcine kidneys. The observed metabolite trends support its value for real-time metabolic assessment. Cortical catheter placement was successful, however, an additional placement in the medulla could provide additional insights.

References

[1]Bellini MI, Tortorici F, Amabile MI, D'Andrea V. Assessing Kidney Graft Viability and Its Cells Metabolism during Machine Perfusion. Int J Mol Sci. 2021 Jan 23;22(3):1121.

[2] Hamaoui K, Gowers S, Damji S, Rogers M, Leong CL, Hanna G, Darzi A, Boutelle M, Papalois V. Rapid sampling microdialysis as a novel tool for parenchyma assessment during static cold storage and hypothermic machine perfusion in a translational ex vivo porcine kidney model. J Surg Res. 2016 Jan;200(1):332-45.

34

The effect of Felzartamab on Natural Killer Cells *in vitro*

Daniela M. Allmer[1], Katharina A. Mayer[1], Susanne Haindl[1], Donna Flesher[2], Tess Delfino[2], Martina Schatzl[1], Stephanie Winter[3], Michael B. Fischer[3], Hannes Vietzen[4], Georg A. Böhmig[1]

[1]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[2]Biogen, South San Francisco, CA, USA
[3]Department of Transfusion Medicine and Cell Therapy, Medical University of Vienna
[4]Center for Virology, Medical University of Vienna, Vienna, Austria

Background

In a recent phase 2 trial, targeting CD38 with the monoclonal antibody felzartamab led to resolution of antibody mediated rejection activity in biopsies from 82% of patients compared to 20% of placebo patients. High CD38 expression on natural killer (NK) cells and their depletion in treated patients suggest that interference with donor-specific antibody-dependent (DSA) and independent NK cell-mediated graft injury may be a key mechanism of action (MOA). However, the exact MOA of NK cell depletion remains unclear. It could involve different mechanisms of antibody-induced apoptosis, including Fc receptor-mediated NK cell "fratricide" via antibody-dependent cellular cytotoxicity (ADCC). The present in vitro experimental study was designed to dissect the mechanisms underlying felzartamab-induced NK cell interference.

Methods

To analyze induction of cell death, peripheral blood NK cells, isolated by negative selection from healthy blood donors, were cultured for 48 hours with increasing concentrations (0.8-500 µg/mL) of felzartamab. In further

experiments, cells were cultured at 100 μg/mL felzartamab in the presence of 10 ng/mL IL-2. Apoptosis was evaluated via flow cytometry, employing an Annexin V/7-AAD staining. Moreover, 19 molecules linked to NK cell activation and degranulation were examined in the cell culture supernatants via the Luminex-platform.

Results
Flow cytometric analysis revealed that felzartamab triggered apoptosis of a subset of NK cells (approximately 31%) at clinically-relevant concentrations. Luminex-based analysis of culture supernatants did not indicate NK-cell degranulation, however, elevated levels of pro-inflammatory cytokines such as MIP1-beta, IL-8, MCP-1, IL-13 and MIP1-alpha were observed. The addition of IL-2 to cultures enhanced felzartamab-triggered apoptosis as well as IFNγ and granzyme B release.

Conclusions
Our results suggest that felzartamab-mediated NK cell depletion may not primarily depend on ADCC-mediated fratricide. Instead, alternative molecular mechanisms might underlie the profound decrease in circulating NK cells in vivo.

Prophylactic Ureteral Stent Placement And BK Polyomavirus Infection After Renal Transplantation – A Retrospective Case-Control Study

Haris Omić[1], **Simon Hoffmann[1]**, Robert Strassl[2], Daniela Gerges[1], Michael Eder [1], Shahrokh F. Shariat[3], Zeljko Kikić[3]

[1]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[2]Department of Virology, Medical University of Vienna, Vienna, Austria
[3]Department of Urology, Medical University of Vienna, Vienna, Austria

Background
BK polyomavirus (BKPyV) infection poses a significant challenge in the management of kidney transplant (KTX) recipients, potentially leading to BKPyV-associated nephropathy (BKPyVAN) and graft loss. Recently, the placement of a prophylactic ureteral stent (UrSt) after KTX has been recommended as the standard of care. UrSt placement is a suggested risk factor for BKPyV-DNAemia; however, this effect may also be influenced by UrSt indwelling time. This study hypothesized that the dose-dependent relationship between UrSt indwelling time is a major driver of the risk of BKPyV-DNAemia in kidney transplant recipients.

Methods
We included all KTX recipients at the Medical University of Vienna with detectable BKPyV-DNAemia from 2010 to 2021. Patients without detectable BKPyV-DNAemia were included as controls. In this nested, retrospective, matched case−control study, matching was performed at a rate of 1:1 according to sex and age at KTX.

Results
Among the 438 KTX recipients, 52.3% of patients who developed BKPyV-DNAemia had received a UrSt, compared to 46.8% of those who remained BKPyV-DNAemia-negative. UrSt placement was not associated with BKPyV-DNAemia in univariable analysis (OR 1.20; 95% CI 0.83−1.75; p = 0.34), but UrSt indwelling time of more than eight weeks was found to significantly increase the risk of BKPyV-DNAemia (OR 1.79; 95% CI 1.10−2.93; p = 0.02). In multivariate analysis, UrSt indwelling time for more than eight weeks remained an independent predictor of BKPyV-DNAemia (adjusted OR: 1.74; 95% CI: 1.06−2.86; p = 0.03).

Conclusions
Overall, prophylactic UrSt placement after KTX was not associated with BKPyV-DNAemia, which supports the current EAU recommendations of prophylactic UrSt placement. However, indwelling of the UrSt beyond eight weeks significantly increased the risk of BKPyV-DNAemia. These findings provide evidence for a strong recommendation to remove prophylactic UrSt within the first eight weeks post-transplant to avoid clinically meaningful BKPyV complications.

Long Term Monitoring Of Torque Teno Virus Load For The Detection Of Infections In Kidney Transplantation

Sebastian Kapps[1], Frederik Haupenthal[1], Konstantin Doberer[1], Gregor Bond[1]

[1]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria

Background

Personalized immunosuppression is crucial to prevent organ rejection and infections in kidney transplant recipients. Plasma load of the non-pathogenic and highly prevalent torque teno virus (TTV) has been suggested to assess the state of immunosuppression. A cut-off value for risk prediction of infections in the first year post-transplant has been defined while cut-off values beyond year one post-transplant are crucial for the design of randomized clinical trials and long term routine clinical care.

Methods

All adults who underwent a kidney transplantation between January 1st and December 31st, 2019 at the Medical University of Vienna were included and followed up for 4 years. Over this time, all infectious events with respective treatments, hospitalizations and changes of immunosuppression were recorded. Infectious disease work up included syndromic PCR panel testing including SARS-CoV-2 PCR. TTV load was measured by PCR from plasma.

Results

This analysis includes 145 patients (37.2% female; median age 55.4 years) experiencing 621 infectious events. Of all events the majority were urinary tract infections (204; 32.9%), 178 of all events led to hospitalization. During the first year TTV load before an infectious event was significantly higher than when outside of 100 days of an infection (8.2 $\log_{10}$ vs. 7.2 $\log_{10}$; *p=0.015*), with the strongest

association for commensal viral infections. From the second year onward no association was found.

Conclusions

While verifying known TTV load cutoffs in a new cohort, this analysis fails to show an association of TTV with infections from the second year after transplantation onwards. This suggests the importance of an additive endpoint such as malignancy and greater sample sizes owed to the overall lower event rate after the first year. In the process of infection workup this work also gives a comprehensive overview of respective treatments, pathogens and hospitalizations in a single center cohort over 4 years.

First Clinical Experience With Maribavir For Refractory CMV-Infection In Kidney Transplant Recipients

Rahel Jagoditsch[1], Stefan Steinringer[1], Christopher Kaltenecker[2], Leon Höllhuber[1], Julius Wenzler[1], Robert Strassl[3] and Farsad Eskandary[1]

[1]Department of Nephrology and Dialysis, Division of Medicine III, Medical University of Vienna, Vienna, Austria
[2]Department of Pathology, Medical University of Vienna, Vienna, Austria
[3]Department of Virology, Medical University of Vienna, Vienna, Austria

Background

Cytomegalovirus (CMV) remains a challenging infectious disease complication after kidney transplantation especially within the CMV high-risk population (CMV-IgG D+/R-). Standard agents for prophylaxis and/or treatment may show significant toxicity and dosing is often complicated by fluctuating renal function. Maribavir, a novel UL97 kinase inhibitor, has recently been approved for treatment-refractory and/or resistant CMV infection/disease and offers a promising alternative treatment modality.

Methods

We report our first clinical experience with Maribavir in a cohort of 9 kidney transplant recipients treated at the Medical University of Vienna since its approval in January 2023. All patients received Maribavir following virological or clinical failure with/without proven resistance of conventional therapy.

Results

Median age at Maribavir initiation was 56years(IQR 45-65), 23% were female and 78% were CMV high-risk constellations. Time from transplantation to first positive CMV-PCR was 33 days (IQR 20-114) and median CMV-load at Maribavir start was 12000c/mL (IQR: 2600-27800), respectively. Median number of anti-CMV treatments before Maribavir was 1(IQR 1-2) with 100% of infections being treatment-refractory/resistant or showing proven genetic resistance in 78%. Median duration of Maribavir treatment was 49.5days (IQR 19-64.5) with 45% reaching sustained viral clearance (<100c/mL on two consecutive measurements one week apart) after 57days (IQR 24-73) days of treatment within the first Maribavir cycle. We detected Maribavir resistance in one patient at a typical site of the UL97 kinase (T409M, H411Y), which prompted us to switch to Letermovir. Dysgeusia was recorded in 23% and one patient died of hepatic failure during treatment with unexplainable but chronologic correlation to Maribavir, but who also suffered from concomitant primary EBV infection.

Conclusions

Our early experience indicates that Maribavir may represent an effective option for the management of refractory/resistant CMV infections after kidney transplantation. Preliminary observations suggest overall good tolerability of Maribavir except for one case of hepatic failure of unknown etiology.

Health-Related Quality of Life in the First Year Post Kidney Transplantation – a Cohort Study

Frederik Haupenthal[1], Habiba Ahmed[1], Konstantin Doberer[1], Sebastian Kapps[1], Bettina Gober[2], Katharina Ebenberger[3] and Gregor Bond[1]

[1]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Austria
[2]Division of Transplantation, Department of General Surgery, Medical University of Vienna, Austria
[3]Department of Cardiac Surgery, Medical University of Vienna, Austria

Background

The improvement of health-related-quality-of-life (HRQOL) remains a main goal after kidney transplantation. An in-depth understanding of individual factors affecting HRQOL might help to develop strategies to support the process of HRQOL improvement. The AdTorque study was designed to assess HRQOL in regard of patient-related characteristics.

Methods

This cohort study screened all 283 consecutive adult kidney graft recipients transplanted at the Medical University of Vienna from 2018 to 2019. HRQOL was monitored within the first-year post-transplant applying the WHOQOL-BREF questionnaire at 3 visits: the first out-patient visit (P1), 3 months (P2) and 12 months post-transplant (P3). The WHOQOL-BREF assesses the HRQOL in the previous month in 4 domains: physical health, psychological health, social relationships and environmental health. Each domain is scored between 0 and 100. A total score for overall HRQOL is calculated by the sum of all domains (0-400). For subgroup analysis all patients were stratified according to sociodemographic, psycho-social and transplant-related variables.

Results

In the total cohort of 183 patients (33% females; median age 56 [IQR 46-53]) the median overall HRQOL was 315 (IQR 278-340) at P1, 322 (IQR 277-351) at P2 and 328 (IQR 289-359) at P3. A significant improvement was only detected in the physical health domain (71 [IQR 54-79] at P1 to 79 [IQR 56-89] at P3; p=0.006). While male sex, younger age and donation from a living donor indicated a positive influence, smoking and living-alone affected the improvements in HRQOL negatively. Patients with psychological disorders (n=67; 37%) reported a significantly reduced HRQOL compared to patients without such disorders (279 [IQR 251-323] vs. 329 [IQR 307-347, p<0.001] at P1, 284 [IQR 244-335] vs. 333 [IQR 297-354, p<0.001] at P2 and 302 [IQR 267-335] vs. 354 [IQR 307-371, p<0.001] at P3).

Conclusions

Patients with a psychological disorder perceived less improvement in their HRQOL post kidney transplantation. Our results emphasize the need for psycho-social support in post-transplant care.

39

Refining HLA Antibody Assessment In Kidney Transplantation: A Novel Approach Using Adsorption And Elution Techniques To Reclassify Unacceptable Antigens

Daniela Koren[1], Daniela Kriks[1], Tanja Mayer[1], Vanessa Spiegl[1], Lisa Sturm[1], Gottfried Fischer[2]

[1]Department of Transfusion Medicine and Cell Therapy, HLA-Laboratory, General Hospital Vienna, Vienna, Austria
[2]Department of Transfusion Medicine and Cell Therapy, Medical University of Vienna, Vienna, Austria

Background

The presence of HLA antibodies in recipients remains a significant immunological challenge in kidney transplantation. Accurate detection and interpretation of these antibodies are essential for assessing immunological risk and determining transplant eligibility.

However, the mere presence of certain HLA antibodies often leads to their classification as unacceptable by current testing strategies, even though they might not be clinically significant. This in turn might unnecessarily limit transplant opportunities for sensitized patients, underscoring the importance of advanced methods for a more nuanced assessment of their clinical relevance.

Methods

We incubate patient serum with lymphocytes expressing various HLA types, followed by acid elution of the bound antibodies. The eluted antibodies are then analyzed using solid-phase assays.

Results

We present several cases demonstrating how this approach refines antibody specificity.

Conclusions

This method enables a more precise assessment of the specificity of the antibody and therefore may lead to a reclassification of certain HLA antibodies previously deemed unacceptable. Consequently, the calculated virtual panel reactive antibody (vPRA) could be lowered, potentially increasing transplant opportunities for sensitized patients.

Histidine-Tryptophan-Ketoglutarate (HTK) As Perfusion Solution During Hypothermic Oxygenated Machine Perfusion (HOPE) Prior To Kidney Transplantation - Case Series

Robert Karitnig, Mauritz Merra, Michael Sereinigg, Robert, Sucher, Philipp Stiegler

Department of General-, Visceral- and Transplant-Surgery, Medical University of Graz, Vienna, Austria

Introduction

Hypothermic oxygenated machine perfusion (HOPE) is an innovative technique to improve outcomes in kidney transplantation by mitigating ischemia− reperfusion injury and extending preservation times. Traditionally, the University of Wisconsin (UW) solution is used as the standard perfusate for machine perfusion, while histidine-tryptophan-ketoglutarate (HTK) solution is widely applied for static cold storage. Using HTK for both static storage and HOPE may simplify the organ processing workflow by eliminating the need to switch preservation solutions, potentially saving time and reducing handling.

Objectives

This case series evaluated the feasibility and clinical outcomes of using HTK as the perfusate during HOPE for kidney grafts. From November 2024 to June 2025, eleven kidneys retrieved and stored in HTK were perfused on the HOPE system using HTK prior to transplantation. We analyzed perfusion time, cold ischemia time (CIT), recipient demographics, serum creatinine trends, and postoperative outcomes. Early allograft dysfunction (EAD) was defined as the need for dialysis after transplantation.

Results

Eight kidney transplants were performed using HOPE with HTK. All grafts came from brain-dead donors (five meeting extended criteria), aged 24−69 years. CIT ranged from 270 to 1,620 minutes, and HOPE lasted 660−1,230 minutes. Recipients (six males, two females) were aged 12−76 years; six were on dialysis preoperatively. Surgery was uneventful in all cases, with operative times of 130−273 minutes and hospital stays averaging 15 days. Three patients experienced delayed graft function requiring temporary dialysis (maximum seven days). From postoperative day 7, all recipients showed a marked decline in serum creatinine, which continued to improve at one and two months. No further dialysis was required during follow-up.

Conclusion

HOPE with HTK appears to be a viable alternative to UW, supporting extended preservation and good postoperative graft function. Serum creatinine normalized within one week in most recipients, with acceptable rates of delayed graft function.

05_Liver Transplantation

41

Ex Vivo Treatment With Norucholic Acid During Normothermic Machine Perfusion Improves Viability, Reduces Perfusate Apoptosis Markers, And Regulates Gene Expression In Livers Declined For Transplantation

Laurin Rauter[1], Jule Dingfelder[1,2], Dagmar Kollmann[2], Nikolaus Becker[1], Sertac Kacar[1], Moriz Riha[1], Effimia Pompouridou[1], Konstantinos Mengrelis[1], Markus Wahrmann[3], Raphael Gronauer[4], Natalia Warmuzińska[5], Kamil Luczykowski[5], Andreas Salat[1], Gerd Silberhumer[1,2], Thomas Soliman[1], Hubert Hackl[4], Matthias Hackl[6], Emina Halilbasic[7], Claudia Fuchs[7], Barbara Bojko[6], Gabriela Berlakovich[1], Michael Trauner[7], David Pereyra[1,2] and Georg Györi[1]

[1]Department of General Surgery, Division of Transplantation, Medical University of Vienna, Vienna, Austria
[2]Department of General Surgery, Division of Visceral Surgery, Medical University of Vienna, Vienna, Austria
[3]Department of Internal Medicine III, Division of Nephrology and Dialysis, Medical University of Vienna, Vienna, Austria
[4]Institute of Bioinformatics, Biocenter Innsbruck, Medical University of Innsbruck, Innsbruck, Austria
[5]Department of Pharmacodynamics and Molecular Pharmacology, Faculty of Pharmacy, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń, Poland
[6]TAmiRNA GmbH, Vienna, Austria
[7]Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria

Background

Normothermic machine perfusion offers a platform for ex vivo therapy of donor organs. Norucholic acid (NCA) has been studied for the treatment of cholestatic and metabolic liver diseases, utilizing its cholehepatic shunting, anti-inflammatory and anti-fibrotic properties. This study investigated ex vivo NCA therapy in declined extended criteria donor (ECD) livers.

Methods

Eighteen livers declined after viability assessment during NMP were analyzed, nine of which received treatment with NCA after two hours. Bile and perfusate composition were analyzed for viability assessment. Liver biopsies were collected pre- and post-NMP for total RNA sequencing and chemical biopsies for metabolomic analysis were collected pre-NMP, at two and twelve hours via solid-phase-micro-extraction fibers.

Results

NCA improved bile biochemistry and injury markers. After treatment with NCA, more livers met transplant criteria at twelve hours (8/9 vs. 3/9, p=0.049). Further, NCA treated livers showed a relative dynamic reduction of perfusate apoptosis markers after six hours (Bcl-2 p=0.040; active Caspase-3; p=0.018; cleaved PARP p=0.024; Cytochrome c p=0.030). The number of pre- to post-NMP differentially expressed miRNAs (32 vs. 10) and mRNAs (554 vs. 203) increased in the NCA treated group. Further sequencing analysis revealed a treatment effect on genes involved in inflammation, heat shock and stress response (down) as well as, interferon signaling and anti-apoptotic genes (up). Gene set enrichment analysis presented treatment interaction enrichment for interferon signaling genes (positive) and angiogenesis, hypoxia and epithelial-mesenchymal transition (negative). Metabolomic analysis showed accumulation of the small peptide Tyr-Leu-Leu-Phe following NCA treatment (FDR<0.001).

Conclusions

Our results demonstrate improved liver viability following ex vivo NCA treatment, with eight of nine livers meeting transplant criteria. Further, they shine light on possible mechanisms including anti-apoptotic effects and regulation of several relevant gene pathways. These findings highlight the potential to improve outcomes of ECD liver grafts through ex vivo therapy with NCA during NMP.

Assessing The Impact Of Normothermic Liver Machine Perfusion On Transplant Timing And Outcomes

A Retrospective Single-Center Analysis

Lukas Prommegger[1], Felix Julius Krendl[1], Benno Cardini[1], Alexander Kofler[1], Florian Ponholzer[1], Franka Messner[1], Thomas Resch[1], Annemarie Weissenbacher[1], Manuel Maglione[1], Christian Margreiter[1], Stefan Schneeberger[1], Rupert Oberhuber[1]

[1]Department of Visceral, Transplant and Thoracic Surgery, Center for Operative Medicine, Medical University of Innsbruck, Innsbruck, Austria

Background

Normothermic liver machine perfusion (NLMP) has emerged as a clinical routine in liver transplantation (LT). Among other benefits, NLMP offers notable logistical advantages by enabling prolonged preservation without adding additional cold ischemia time, facilitating a shift to daytime transplantation. The objective of this study was to assess the impact of transplant timing (daytime vs. nighttime) on posttransplant outcomes and potential downstream effects.

Methods

All adult LT between February 2018 and January 2024 were included. Daytime LT was defined as surgery start between 8am-8pm. Outcomes were compared for day- vs. nighttime LT, as well as benchmark and non-benchmark cases. Survival analysis was performed using Kaplan-Meier-plots and the log-rank test. Binary logistic regression analysis was applied to assess the effect of clinical parameters on posttransplant outcomes.

Results

Of the 387 LT included, 222 (57%) underwent NLMP and 165 (43%) were transplanted following SCS. Overall, 81% of LT were performed as daytime surgery. The percentage of nighttime LT decreased from 42% in year one to 4% in year five and 10% in year six. NLMP usage increased significantly over the study period from 24% in year one to 87% in year six. The one-year graft survival rate was similar for day- and nighttime LT (84%, nighttime LT: OR 0.90, 95% CI 0.42 - 1.95). In the overall cohort the one year graft survival rate was 94% for benchmark cases.

Conclusions

NLMP allows to move LT out of the night, essentially converting an emergency surgical procedure into a (semi-)elective one. However, while transforming LT into a scheduled daytime operation may help address hospital staff burnout and workforce attrition, thereby fostering a more sustainable transplant program, patient outcomes did not differ for day- vs nighttime LT.

Evaluating Liver Transplantation As A Curative Approach In Metastatic Gastrointestinal Neuroendocrine Tumors: A Case Series

Todor Stoyanov, Lorenz Kircher, Saulius Mikalauskas, Andri Lederer, Robert Sucher, Daniela Kniepeiss, Zoltan Mathe

Department of General-, Visceral- and Transplant Surgery, Medical University of Graz, Graz, Austria

Background

Neuroendocrine tumors of gastrointestinal origin (GI-NETs) frequently metastasize to the liver. In selected patients with unresectable tumors, liver transplantation has emerged as a potential curative option. This case series examines clinical benefits and surgical outcome of liver transplantation in patients with liver metastases of GI-NETs in our center.

Methods

We retrospectively analyzed data from 5 patients (male n=4, mean age 50.2 (28-67) years) who underwent liver transplantation for liver metastases of a GI-NET at our center between 2020 and 2025. The primary tumor was located in the pancreas (n=2), in the ileum (n=2) and in the stomach (n=1). All patients were selected for liver transplantation based on the Milan-NET criteria. Pre-operative evaluation included abdominal computed tomography (CT) and functional imaging with Gallium-DOTANOC PET scan. Somatuline (lanreotide) was used as a conservative therapy for symptom control and tumor growth inhibition in all patients. Liver transplantation was performed in bicaval (n=2) or piggyback technique (n=3). Immunosuppression was initially based on a standard triple regimen and subsequently switched to Everolimus.

Results

All procedures were completed without significant intraoperative or perioperative complications. One patient required surgical revision due to an abdominal wall infection. The median operation time was 271 minutes (range: 197–322 minutes). The mean duration of hospitalization was 15.4 (8–25) days. Postoperative follow-up encompassed standardized graft function assessment alongside routine imaging surveillance to detect potential disease recurrence. During follow-up, all patients maintained a favorable clinical status with no evidence of primary disease recurrence.

Conclusion

Liver transplantation represents a safe and potentially curative treatment option for patients with isolated hepatic metastases from GI-NETs, offering good outcomes and sustained quality of life. Careful patient selection and timing are critical to optimize outcomes in this highly specialized indication.

Liver Transplantation For Polycystic Liver Disease

Lorenz Kircher, Daniela Kniepeiss, Todor Stoyanov, Philipp Stiegler, Andri Lederer, Christian Margreiter, Robert Sucher, Zoltan Mathe

Department for General, Visceral and Transplant Surgery, Medical University of Graz, Graz, Austria

Background

Liver transplantation for polycystic liver disease (PLD) is generally reserved for severe, symptomatic cases that are refractory to medical and surgical therapy. The main indications for liver transplantation include massive hepatomegaly leading to mechanical complications and poor quality of life, combined with malnutrition or cachexia, respiratory compromise, recurrent cyst infections and failure of other interventions. PLD is usually associated with autosomal dominant polycystic kidney disease (ADPKD) or autosomal dominant polycystic liver disease (ADPLD).

Methods

We retrospectively analysed data from seven patients (male n=3, age 34-63 years) with polycystic liver disease, who underwent liver transplantation at our centre between 2015 and 2025. Indications for listing were symptomatic discomfort, loss of weight or failure to reduce symptoms after paracentesis. Liver function was well preserved in all patients. The liver transplantation was performed using either the bicaval (n=2) or the piggyback (n=5) technique. The size of the explants posed a significant intraoperative challenge yet was manageable through partition of the organ before resection.

Four patients received kidney transplantation either prior to (n=3) or simultaneously with (n=1) liver transplantation.

Results

All procedures were completed without intraoperative complications. Operation times ranged from 4.5 to

6 hours. The graft weights varied between 2.8 kg and 17.4 kg, with a mean weight of 6.9 kg. No malignancy was found in any of the explants. Median postoperative ICU stay was 8d (3-21) and hospital stay 35d (11-79). One case of subacute rejection and postoperative bleeding was managed with corticosteroid therapy and operative revision, this patients stay doubled all others ICU stay and hospitalisation days. At discharge and throughout the follow-up period, all patients maintained excellent general condition and graft function.

Conclusions

Liver transplantation is a safe and effective treatment for selected patients with symptomatic polycystic liver disease, offering significant symptom relief and improved quality of life.

45

Evaluation Of Selected MicroRNAs During Normothermic Machine Perfusion Allows For Prediction Of Outcome After Liver Transplantation

Lisa Kamauf[1], Jule Dingfelder[1,2], Laurin Rauter[1], Nikolaus Becker[1], Moriz Riha[1,2], Matthias Hackl[3], Patrick Starlinger[4], Gabriela Berlakovich[1], Georg Györi[1] and David Pereyra[1,2]

[1] Department of General Surgery, Division of Transplantation, Medical University of Vienna, Austria
[2] Department of General Surgery, Division of Visceral Surgery, Medical University of Vienna, Austria
[3] TAmiRNA GmbH, Vienna, Austria
[4] Department of Surgery, Division of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, MN, USA

Background

Normothermic machine perfusion (NMP) has emerged as a viable tool to asses marginal liver grafts prior to transplantation. However, reliable, easily assessable and non-invasive biomarkers to predict postoperative graft function are still lacking. This study investigates the predictive potential of perfusate-derived microRNAs (miRNAs) during NMP for graft viability and postoperative outcome.

Methods

Organs undergoing NMP between 2021 and 2024 at the Medical University of Vienna were included in this study. Perfusate samples were collected at baseline, after 5 and after 60 minutes of perfusion. MiRNAs 122-5p, 151a-5p, and 192-5p were quantified using the commercially available hepatomiR® Kit. In transplanted grafts, the incidence of early allograft dysfunction (EAD) was assessed according to the criteria established by Olthoff et al.

Results

A total of 33 livers were evaluated, of which 22 grafts (66.7%) were transplanted. Among the 22 transplanted grafts, 15 livers (68.2%) developed EAD. There were no significant differences in miRNA levels between transplanted and discarded grafts. However, miRNA levels were significantly elevated in grafts that developed EAD. Specifically, miRNA-122-5p was higher after 60 minutes (p = 0.007), miRNA-151a-5p after 5 minutes (p = 0.026) and 60 minutes (p = 0.005), and miRNA-192-5p after 5 minutes (p = 0.021) and 60 minutes (p = 0.003). ROC analysis showed the highest predictive accuracy for EAD after 60 minutes of NMP, with an AUC of 0.857 for miRNA-122-5p, 0.867 for miRNA-151a-5p, and 0.886 for miRNA-192-5p. These values exceeded those of conventional parameters such as perfusate AST (AUC 0.833) or LDH (AUC 0.786), while lactate didn't show a predictive potential for EAD.

Conclusions

MiRNA levels in perfusate during NMP are non-invasive predictors of EAD and outperform established biochemical markers. Incorporating miRNA analysis as a viability assessment tool during NMP could optimize organ selection and improve graft survival after transplantation.

Hypothermic Oxygenated Perfusion Of The Liver With HTK Solution: A Viable Alternative To UW In Single-Strategy Protocols

Moriz Riha[1,2], David Pereyra[1,2], Jule Dingfelder[1,2], Hubert Hackl[3], Julian Flavio Müller[1], Nikolaus Becker[1], Jakob Eichelter[1,2], Gabriela Berlakovich[1], Georg Györi[1] and Thomas Soliman[1]

[1] Department of General Surgery, Division of Transplantation, Medical University of Vienna, Vienna, Austria
[2] Department of General Surgery, Division of Visceral Surgery, Medical University of Vienna, Vienna, Austria
[3] Institute of Bioinformatics, Biocenter, Medical University of Innsbruck, Innsbruck, Austria

Background

Hypothermic oxygenated machine perfusion (HOPE) has shown benefits over static-cold storage (SCS) in liver transplantation. While the University of Wisconsin (UW) solution is the most commonly used perfusion solution, data comparing it to other solutions remains limited. Histidine-tryptophan-ketoglutarate (HTK), known for its cost-efficiency and wide availability, may be suitable for HOPE in a single-solution strategy, as it is not recommended to change organ solutions over the procurement process. This study evaluates whether HTK can match the clinical performance of UW in HOPE while offering mentioned economic and logistical advantages.

Methods

From May 2023 to October 2024, 173 liver transplantations following HOPE were performed. Of these, 23 grafts were perfused using HTK. A propensity score matched cohort of 23 grafts preserved with UW was identified based on donor/recipient characteristics, cold ischemia time, and general HOPE duration. Outcomes included early allograft dysfunction (EAD), biliary compli-

cations within 6 months, need of postoperative dialysis, and perfusion cost calculation.

Results

Postoperative outcomes were comparable in regard to ICU stay (HTK: 8 days vs UW: 9 days, p=0.760), hospitalization (HTK: 23 vs UW: 21 days, p=0.742), and comprehensive complication index (HTK: 33.5 vs UW: 36.5, p=0.740). EAD occurred equally in both groups (47.8%, p=1.000). Interestingly, HTK showed a trend towards reduced rates of postoperative biliary complications (13.0% vs 30.4%, p=0.153) and dialysis (17.4% vs 31.8%, p=0.260). HTK use led to a cost reduction of approximately €500 per perfusion.

Conclusions

HTK appears to be a feasible and cost-effective alternative to UW in HOPE, delivering similar outcomes and trends toward fewer biliary complications and dialysis. Larger prospective studies are needed to confirm these findings and better define HTK's role in HOPE.

A Modified MELD Including HDL Improves The Prediction Of Short-Term Mortality In Acutely Decompensated Cirrhosis

Rudolf E. Stauber[1], Eva Usòn[2], Florian Rainer[1], Vanessa Stadlbauer[1], Hubert Scharnagl[3], Cristina Sánchez-Garrido[2], Gunther Marsche[4], Joan Clària[2], Richard Moreau[2]

[1] Department of Internal Medicine, Medical University of Graz, Graz, Austria
[2] European Foundation for the Study of Chronic Liver Failure (EF Clif), Barcelona, Spain
[3] Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Graz, Austria
[4] Division of Pharmacology, Otto Loewi Research Center, Medical University of Graz, Graz, Austria

Background

Chronic liver failure is associated with multiple lipidomic alterations including markedly reduced high-density lipoprotein cholesterol (HDL-C) levels. We previously demonstrated that HDL-C levels have excellent prognostic value comparable to that of MELD. In the present study we aimed to develop a new prognostic model containing HDL-C and other readily available biomarkers for prediction of 90-day mortality in patients with acutely decompensated (AD) cirrhosis.

Methods

We studied a subset of the European multicentre CANONIC and PREDICT cohorts in whom HDL-C was retrospectively measured in stored plasma samples. HDL-C and other prognostic variables available in the EF-CLIF database were evaluated. Multivariable competing risk analysis was performed with death as the event of interest and liver transplantation as a competing risk. Cox proportional hazards regression was used to construct a new prognostic model and its performance was evaluated using Harrell's concordance index (c-index) and compared that of MELDNa, MELD 3.0 and CLIF-C AD score by the Integrated Discriminating Improvement (IDI) statistics test.

Results

We analyzed 823 patients with AD (median age 59 years; 69% male; etiology alcohol 58%; 90-day mortality 15%). Multivariable analysis identified 6 independent prognostic variables associated with 90-day mortality, i.e. age, HDL-C, creatinine, sodium, WBC and INR, that were incorporated in the new prognostic model termed integrated MELD (iMELD)-HDL. The new model showed superior discrimination ability for prediction of 90-day mortality by c-index (95% CI) as compared to existing prognostic scores: iMELD-HDL 0.75 (0.71-0.79); MELDNa 0.70 (0.65-0.74, p<0.001 vs. iMELD-HDL); MELD 3.0 0.70 (0.66-0.74, p<0.001 vs. iMELD-HDL); CLIF-C AD score 0.71 (0.67-0.76, p<0.001 vs. iMELD-HDL).

Conclusions

A new prognostic iMELD-HDL model yielded superior accuracy for prediction of short-term mortality as compared to existing prognostic scores. External validation in large cohorts of patients with AD cirrhosis and/or waitlisted for liver transplantation is warranted.

Predictive Capacity Of MicroRNAs During Ex Situ Normothermic Machine Perfusion Of Human Livers

Julia Hofmann[1], Matthias Hackl[2], Susanna Skalicky[2], Stefan Schneeberger[1], Patrick Starlinger[3], Theresa Hautz[1]

[1] organLife Organ Regeneration Center of Excellence and Daniel Swarovski Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria
[2] TAmiRNA GmbH, Vienna, Austria
[3] Department of Surgery, Division of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, Minnesota, USA

Background

Normothermic machine perfusion (NMP) enables assessment of liver graft function prior to transplantation. However, standardized and validated biomarkers are still lacking. Circulating microRNAs (miRNAs) have emerged as sensitive indicators of tissue injury and cellular function. This study examined the dynamics of perfusate miRNAs during liver NMP and their association with clinical and biochemical parameters.

Methods

Human livers (N=44) underwent NMP for up to 24 hours. Serial perfusate samples were collected at 1, 4, 6, and 12 hours, as well as at the end of NMP, for routine laboratory analysis. The hepatomiR® kit (TAmiRNA) was used to quantify perfusate levels of miR-151a-5p, miR-122-5p, and miR-192-5p. Outcomes of transplanted livers were evaluated based on the incidence of early allograft dysfunction (EAD).

Results

In the discovery phase, analysis of 120 perfusate samples from 24 individual liver perfusions revealed significant differences in miRNA levels between transplanted and non-transplanted livers at all time points. Notably, these

differences were already apparent at 1 hour of NMP for all assessed miRNAs (miR-151a-5p: p=0.0002; miR-122-5p: p=0.0003; miR-192-5p: p<0.0001). These findings were validated in a separate cohort (N=20), where significantly higher levels of miR-151a-5p (p=0.0075), miR-122-5p (p=0.0202), and miR-192-5p (p=0.0191) were observed in non-transplanted livers at 1 hour of NMP compared to transplanted livers. Furthermore, miR-122-5p levels at the end of NMP were associated with posttransplant EAD (p=0.0165).

Conclusion

Perfusate miRNA measurement using the hepa-tomiR® kit during NMP offers a reliable approach for assessing liver quality and predicting early graft function after transplantation. Importantly, significant miRNA differences can be detected as early as 1 hour into NMP.

49

Metabolic Microdialysis During Normothermic Machine Perfusion Of The Liver

Dullnig Michael[1], Mathis Simon[1], Putzer Gabriel[1], Resch Thomas[2], Martini Judith[1]

[1]Department of Anesthesiology and Critical Care Medicine, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria

Background

Normothermic machine perfusion (NMP) of liver grafts prior to transplantation enables monitoring of organs, a more differentiated decision on transplantation and increases the probability of transplantation.[1]Micro-dialysis (MD) is a method in which a probe is inserted into the target organ, allowing the measurement of metabolite concentrations in the extracellular space via a semi-permeable membrane.[2] In this project, the technical applicability of MD during NMP of a liver is tested with the aim of recording a lactate profile in the extracellular space.

Methods

Nine porcine livers were treated with NMP using a Metra device (OrganOx). After initiation of NMP the MD catheter was guided into the box and inserted into the right liver lobe. Lactate MD measurements were conducted every 20 minutes for the first two hours and then every hour for 22 hours. In parallel, lactate was measured in perfusate and compared with values obtained from the MD measurements using Spearman rank correlation.

Results

9 NMP porcine livers were included in the study. In six grafts, a drop in lactate during the first five hours of perfusion was detected in the extracellular space, reaching values below 10% of baseline (Figure 1). MD lactate values correlated with lactate values measured in perfusate with an average coefficient of 0.9. Interestingly, one graft showed an increase in MD lactate concentration, which did not correlate with lactate concentrations measured in perfusate. (Figure 1, Red Line) Therefore MD seems to be preferable to a pure concentration measurement in the perfusate, as local metabolic changes may be better detected.
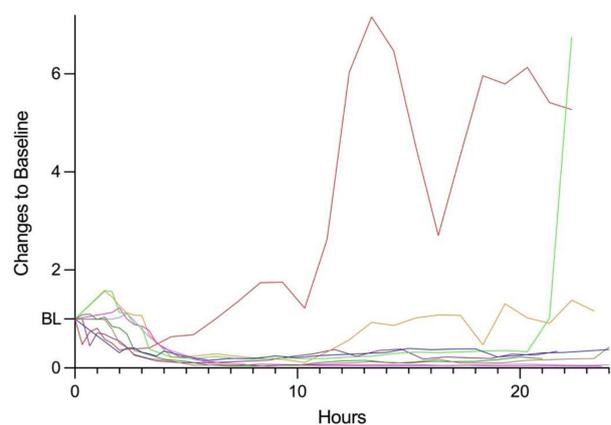

Figure 1 | Relative lactate changes during NMP of the liver

Conclusion

Our data demonstrate that MD is an effective method for monitoring metabolic processes of a liver graft during NMP. Furthermore, they also suggest that measurement of lactate by MD may be superior to the measurement of lactate in perfusate, particularly in specific situations.

References

[1] Nasralla D, et al. A randomized trial of normothermic preservation in liver transplantation. Nature. 2018 May;557(7703):50-56. doi: 10.1038/s41586-018-0047-9. Epub 2018 Apr 18. PMID: 29670285.

[2] Håugaa H, et al. Early bedside detection of ischemia and rejection in liver transplants by microdialysis. Liver Transpl. 2012 Jul;18(7):839-49. doi: 10.1002/lt.23425. PMID: 22407878.

06_Lung Transplantation

50

Evaluation Of Stress Index As New Parameter For Protective Ventilation Strategies During Clinical Ex-Vivo Lung Perfusion

Panja M. BOEHM[1], Sophia AUNER[1], Jakob HOMOLA[1], Caroline HILLEBRAND[1], Shahrooz NASROLLAHI-SHIRAZI[1], Alexis SLAMA[1], Stefan SCHWARZ[1], Peter JAKSCH[1], Clemens AIGNER[1], Alberto BENAZZO[1]

[1]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

During ex-vivo lung perfusion (EVLP), lungs are perfused and ventilated outside the protective confines of the rib cage, making ventilation settings particularly challenging. This increases the importance of applying protective ventilation strategies. The stress index (SI), the dynamic pressure-time curve, is used in intensive care, and can help detect lung overinflation in real time (defined as SI>1). This study presents our first experience collecting stress index data during clinical EVLPs.

Methods

According to the Vienna EVLP protocol, donor lungs were ventilated with 7mL/kg body weight with FiO2 0.21 and PEEP 7. Ventilation started at 32 degrees of perfusate temperature with volume-targeted pressure-controlled ventilation. During hourly oxygen challenges and recruitment, PEEP and FiO2 were increased to 10 and 1.0 for 10 minutes before blood gas analysis. Standard ventilation parameters were continuously recorded, including mean (Pmean) and peak pressure (Ppeak), static (Cst) and dynamic (Cdyn) compliance, and inspiratory (VTi) and expiratory (VTe) tidal volumes. Stress index was also measured continuously.

Results

Stress index data was collected during six clinical EVLP runs. Five lungs (83%) were accepted for transplantation after EVLP, while one was declined due to edema and insufficient oxygenation. Duration of EVLP was six hours for all cases. Median stress index was always below 1, both during regular ventilation and recruitment (range 0.846-0.988). Stress index was lower during regular ventilation (SI=0.947, range 0.846-0.983) than during recruitment (SI=0.976, range 0.957-0.986). Spearman correlation coefficient showed a positive weak correlation between stress index and peak pressure (r=0.3).

Conclusions

Based on a small sample size of six cases, our preliminary findings indicate that lungs were not overinflated during EVLP, suggesting that stress index correlates well with a protective ventilation strategy and may be a valuable tool for guiding ventilation during EVLP. Further research is needed to explore its potential in optimizing lung ventilation strategies.

The Use Of Extracorporeal Photopheresis As Immunomodulatory Therapy Of Subclinical Antibody-Mediated Rejection And Chronic Lung Allograft Dysfunction: A Prospective Randomized Controlled Trial (NCT06112951)

Sophia Alemanno, Shahrooz Nasrollahi Shirazi, Oya Hatice Berezhinskij, Peter Jaksch, Alberto Benazzo

Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

Despite significant advances in lung transplantation, long-term outcomes remain limited by the de novo donor-specific antibodies (dnDSAs) which are linked to antibody-mediated rejection (AMR), chronic lung allograft dysfunction, and increased mortality[1]. Our group previously demonstrated that extracorporeal photopheresis (ECP) reduces dnDSAs and stabilizes allograft function after AMR[2]. We now hypothesise that ECP modulates subclinical humoral alloimmunity and promotes graft tolerance. The randomized controlled trial (RCT) investigates the immunomodulatory effects of ECP on B cell responses through in vitro analysis of patient-derived PBMCs and ECP-treated MNCs.

Methods

In this prospective RCT, 80 lung transplant recipients with subclinical AMR are randomized to either a "watch-and-wait" or an ECP group. To date, 16 patients have been enrolled and samples are collected at weeks 1, 9, and 21. B cells are isolated and co-cultured for seven days with ECP-treated MNCs, buffy coat supernatant, or the entire buffy coat, with or without stimulation. B cell phenotype and activation are assessed by flow cytometry.

Results

After 7 days of coculture with ECP products, B cell subset dynamics vary by condition and stimulation. At weeks 1 and 9, unstimulated B cells show decreased memory and double-negative compartments, while stimulation induces plasmablast differentiation. Buffy coat generally enhances antibody-secreting cells, while supernatant often leads to poor cell survival. Preliminary data from 3 patients at week 21 suggest a consistent reduction in memory and naïve B cells, and increased $CD27^-CD38^-IgD^-$ cells, especially after stimulation, indicating sustained immunomodulatory effects over time.

Conclusions

These early findings support a role for ECP in modulating B cell subsets in subclinical AMR, suggesting a shift toward antibody-secreting and class-switched memory phenotypes, while reducing populations associated with naïve and double-negative B cells. These results support the immunomodulatory potential of ECP in regulating humoral alloimmunity. Ongoing analyses will further clarify these mechanisms.

References

[1] Chambers DC, P.M., Zuckermann A, et al, *The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-eighth adult lung transplantation report - 2021; Focus on recipient characteristics.* J Heart Lung Transplant 2021. **40**: p. 1060-72

[2] Benazzo A, Worel N, Schwarz S, et al. Outcome of Extracorporeal Photopheresis as an Add-On Therapy for Antibody-Mediated Rejection in Lung Transplant Recipients. Transfus Med Hemother 2020;47:205-13.

Donations After Uncontrolled Circulatory Death (uDCD) Creates Opportunities For Donor Pool Expansion – Experience With Lung Transplantation In Vienna

Jakob Homola[1], Panja M. Boehm[1], Sophia Auner[1], Shahrooz Nasrollahi-Shirazi[1], Alexis Slama[1], Peter Jaksch[1], Clemens Aigner[1], Alberto Benazzo[1]

[1]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

Lungs from uncontrolled donation after circulatory death (uDCD; Maastricht category II) following unexpected cardiac arrest are considered high-risk due to prolonged warm ischemia but represent a valuable donor source. uDCD lungs are routinely evaluated using ex-vivo lung perfusion (EVLP) to assess function and quality. We present the Vienna experience with lung transplantation after EVLP of uDCD lungs.

Methods

We retrospectively report our experience with uDCD lungs since the start of the Vienna EVLP program in 2010. All donors were managed according to the institutional uDCD protocol, including continued CPR, invasive ventilation, and intravenous heparin prior to procurement. EVLP was performed with normothermic, acellular perfusate. Outcomes of transplanted recipients were analyzed.

Results

Four donors (aged 15, 22, 56, and 56 years) with traumatic injuries underwent EVLP for 2.5 to 5.8 hours. Two lungs were transplanted; two were declined after functional assessment. One declined lung showed dorsal contusions and progressive pulmonary edema during EVLP. The other demonstrated excellent compliance and a delta pO_2 of 350mmHg but was rejected due to significant perfusate loss caused by a segment 10 bronchial laceration, confirmed on post-EVLP dissection. The transplanted lungs (from 15- and 56-year-old female donors) led to favorable clinical outcomes. Both recipients (44 years, CF; 56 years, pulmonary fibrosis) had no signs of primary graft dysfunction at 72 hours, were extubated after 48 and 36 hours, and discharged on postoperative day 15. The 44-year-old survived 2.5 years before developing CLAD. The 56-year-old died after 1.8 years due to infection; follow-up confirmed survival up to 23 months.

Conclusions

uDCD lungs, when systematically evaluated by EVLP, can be safely transplanted with favorable mid-term outcomes. Further development of structured protocols may help expand this promising donor source.

Individualized Flow Controlled Ventilation In Ex Vivo Lung Perfusion

Manuela Ranalter[1], Julia Abram[1], Florian Ponholzer[2], Neuschmid Marie-Christin[2], Patrick Spraider[1], Gabriel Putzer[1], Judith Martini[1]

[1] Department of Anesthesia and Intensive Care Medicine, Medical University of Innsbruck, Innsbruck, Austria
[2] Department of Visceral, Transplantation and Thoracic surgery, Medical University of Innsbruck, Innsbruck, Austria

Background

The XVIVO® system is a normothermic ex vivo lung perfusion (EVLP) device designed to extend preservation times and, potentially enable future therapeutic interventions in extended criteria donor lungs.

Flow controlled ventilation (FCV) is a novel ventilation mode enabling active control of both inspiration and

expiration phases. Due to a constant gas flow throughout the entire ventilation cycle, direct intratracheal pressure measurement becomes feasible. Ventilation can therefore be individualized according to dynamic lung compliance, which might be of primary interest especially in extended criteria donor organs. While individualized flow-controlled ventilation has been shown to improve gas exchange and lung tissue areation in vivo (1, 2), it has not yet been applied in an ex vivo model.

Methods

Lungs procured from domestic pigs weighing 70 kg were prepared and implemented in the ex vivo lung perfusion device. Perfusion was gradually increased to 40 % of predicted cardiac output. Once a temperature of 32 °C was reached, individualized FCV was initiated. Ventilator parameters were adjusted in accordance to dynamic lung conditions, ensuring ventilation within the upper and lower inflection points of the pressure-volume curve to optimize lung protection. Lungs were ventilated for 6 each hours under individualized FCV settings.

Results

Individualized FCV was feasible during EVLP (n=5). Pressure-volume-loops confirmed ventilation within dynamic lung mechanic limits. Previous findings showed reduced mechanical power delivered to the lung, a potential predictor for the development of ventilator-induced lung injury. To further assess the impact of individualized ventilator settings on donor graft quality, a study with individualized FCV compared to lung-protective volume controlled ventilation (VCV) will be conducted.

Conclusions

Individualized flow-controlled ventilation is applicable in an ex vivo setting. A forthcoming study will investigate the impact of individualized FCV versus standard lung-protective VCV on graft quality during prolonged EVLP.

Literature

1. Abram J, Martini J, Spraider P, Putzer G, Ranalter M, Wagner J, et al. Individualised flow-controlled versus pressure-controlled ventilation in a porcine oleic acid-induced acute respiratory distress syndrome model. Eur J Anaesthesiol. 2023;40(7):511-20.
2. Spraider P, Martini J, Abram J, Putzer G, Glodny B, Hell T, et al. Individualized flow-controlled ventilation compared to best clinical practice pressure-controlled ventilation: a prospective randomized porcine study. Crit Care. 2020;24(1):662.

Back-Table Reconstruction Of Partial Anomalous Pulmonary Venous Return In Lung Transplantation

Jakob Hirsch[1], Florian Ponholzer[2], Florian Augustin[2], Christoph Krapf[1]

[1]Department of Cardiac Surgery, Medical University of Innsbruck, Austria
[2]Department of Visceral, Transplantation and Thoracic Surgery, Medical University of Innsbruck, Austria

Background

Partial anomalous pulmonary venous return (PAPVR) is a rare congenital anomaly in which pulmonary veins drain into systemic venous structures instead of the left atrium. While recognized in congenital heart disease, PAPVR is only sporadically reported in the context of lung transplantation, often overlooked during donor evaluation due to imaging limitations. Clear surgical strategies for managing this anomaly in donor lungs are lacking.

Methods

We present the case of a 59-year-old female with end-stage COPD undergoing bilateral lung transplantation. During donor lung assessment, PAPVR of the left upper pulmonary vein was identified, draining into the left subclavian vein and then into the innominate vein. The anomalous vein was excised en bloc with a segment of subclavian and innominate vein. A direct anastomosis between the venous segment and the donor left atrial cuff was performed on the back table, enabling standard implantation.

Results

The transplantation proceeded uneventfully. Postoperative imaging confirmed unobstructed pulmonary venous return. The patient developed transient perioperative atrial fibrillation and was treated short-term with apixaban, later transitioned to low-dose aspirin. No signs

of venous congestion, stenosis, or thrombotic complications were observed during follow-up. Long-term anticoagulation was deemed unnecessary due to stable sinus rhythm and native tissue reconstruction.

Conclusions
This case demonstrates that careful intraoperative donor assessment can identify rare vascular anomalies such as PAPVR. A direct anastomosis to the left atrial cuff enabled successful transplantation without synthetic grafts, minimizing long-term risks. This tailored surgical strategy underscores the importance of flexibility and vigilance in transplant procedures involving unanticipated anatomic variants.

55

Impact Of High-Altitude Exposure On Torque Teno Virus (TTV) Levels And Immunosuppression In Lung Transplant Recipients - Climbing Mt. Jebel Toubkal

Jakob Mühlbacher[1]*, Sebastian Kapps[2], Jarina Fabriova[1], Alexis Slama[3], Lora Schrutka[4] ,Vasiliki Besa[9], Paul Lichtenegger[5], Gieszer Balázs[11], Gerold Ebenbichler[6], Roland Winkler[8], Peter Faybik[5], Clemens Aigner[4], Konrad Hoetzenecker[4], Wilfried Wisser[12], Alberto Benazzo[4], Elisabeth Puchhammer-Stöckl[4], Irene Görzer[4], Stephan Aberle[4], Birgit Reiter[7], Peter Jaksch[4]

[1]Department of Surgery, Division of Visceral Surgery, Medical University of Vienna, Vienna, Austria
[2]Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[3]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria
[4]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria
[5]Center for Virology, Medical University Vienna, Vienna, Austria
[6]Department of Anesthesiology, General Intensive Care and Pain Therapy, Medical University of Vienna, Vienna Austria
[7]Department of Physical Medicine and Rehabilitation, University of Vienna, Austria
[8]Clinical Institute of Laboratory Medicine, Medical University of Vienna, Vienna, Austria
[9]Rehabilitation Center Hochegg for Cardiovascular and Respiratory Diseases, Grimmenstein, Austria
[10]Department of Pneumology, University Medicine Essen-Ruhrlandklinik, University Duisburg-Essen, Essen, Germany
[11]Department of Thoracic Surgery, Semmelweis University, Budapest, Hungary
[12]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

Background
Following successful lung transplantation (LuTx), some patients attain long-term health comparable to healthy individuals, enabling participation in demanding activities such as high-altitude mountaineering. High-altitude exposure induces significant physical stress through hypoxia, exhaustion, and UV radiation, potentially compromising immunocompetence. Immunosuppression and Torque Teno virus (TTV), a persistent, non-pathogenic single-stranded DNA virus associated with the immunocompetence, were measured during an expedition to the highest peak in North Africa.

Methods
Immunosuppression and TTV was monitored in LuTx patients and healthy controls before, during, and after an expedition to Mount Jebel Toubkal (4167m). In order to be able to measure in remote areas, a microsampling device (MSD) was validated in the cohort by comparing capillary blood samples with plasma samples. Levels of immunosuppression were determined using the routinely used LC-MS/MS method, and TTV DNA was quantified using real-time polymerase chain reaction.

Results
At baseline, TTV DNA was detectable in 92.8% of lung transplant recipients (13 of 14) and 83.3% of healthy controls (10 of 12), with a median viral load of 6.81 $\log_{10}$ copies/mL (IQR 5.61−7.18) and 3.15 $\log_{10}$ copies/mL (IQR 2.90−3.59), respectively. TTV load from plasma and MSD showed high correlation (slope: 0.74, Pearson's r: 0.88, R^2:0.78, p>0.001). Comparison of TTV loads before and after the expedition revealed no significant change in either lung transplant recipients (p = 0.998) or controls (p = 0.852). Tacrolimus and everolimus trough levels remained stable during the expedition (p= 0.326 and p=0.894). Linear regression analysis of duplicate MSD measurements showed high concordance for tacrolimus (n=95; slope 0.94, r=0.99, R^2=0.99) and everolimus (n=26; slope 0.96, r=0.99, R^2=0.98; both p<0.001).

Conclusions

Strenuous physical exertion during a mountaineering expedition is safe after LuTX. TTV load and levels of immunosuppressive medication can be measured by MSD during such trips enabling remote immune monitoring of transplant recipients.

56

Extracorporeal Photopheresis Modulates Immune And Erythropoietic Pathways Via GATA2 In Lung Transplant Recipients

Panagiotis Parsonidis[1], Anna Marianne Weijler[1], Ara Cho[1,2], Verena Kainz[1], Sophia Derdak[3], Alberto Benazzo[4], Peter Jaksch[4], Thomas Wekerle[1]

[1] Department of General Surgery, Division of Transplantation, Medical University of Vienna, Vienna, Austria
[2] Department of Dermatology, Medical University of Vienna, Vienna, Austria
[3] Core Facilities, Medical University of Vienna, Vienna, Austria
[4] Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

Chronic lung allograft dysfunction (CLAD) remains the leading cause of late mortality after lung transplantation. Extracorporeal photopheresis (ECP), an immunomodulatory therapy, has shown promise in reducing acute cellular rejection, infections, and CLAD incidence post-transplantation. To investigate the underlying mechanisms, this study applies transcriptomic profiling of peripheral blood mononuclear cells (PBMCs) from lung transplant recipients treated with or without ECP.

Methods

In a randomized, controlled single-center trial, lung transplant recipients received either standard immunosuppression alone (n=30) or with ECP (8 cycles within 3 months, n=30). Bulk RNA sequencing (1x50 bp) was performed on a NextSeq2000 platform using PBMCs from 8 ECP-treated and 8 control patients collected at baseline and at 3 months post-transplant. Reads were aligned to GRCh38 with STAR, and gene expression was quantified with RSEM and analyzed with DESeq2. Gene set enrichment analysis (GSEA) used the MSigDB Hallmark gene sets. Transcription factor enrichment was assessed with Enrichr (ChEA 2016), and protein interaction networks were visualized using Cytoscape and STRING data.

Results

ECP treatment led to distinct gene expression changes at 3 months post-transplantation compared to controls. Differential expression analysis identified upregulation of genes involved in erythropoiesis and heme metabolism. GSEA highlighted pathways associated with erythroid differentiation and immune modulation. Transcription factor enrichment identified GATA2 as a key regulator. A GATA2-centered network revealed direct interactions with targets including GATA1, TRIM58, SPTA1, SPTB, and OSBP2, suggesting a potential role for GATA2 in ECP-mediated immunomodulation.

Conclusions

These preliminary results suggest that ECP induces a previously unrecognized immunological remodeling signature in lung transplant recipients, prominently involving GATA2 and genes linked to erythropoiesis. GATA2 is essential for early erythropoiesis, regulating progenitor cell survival and initiating the erythroid differentiation program. By integrating transcriptomic and protein interaction network analyses, we provide novel insights into mechanisms by which ECP may reduce CLAD, supporting its therapeutic potential.

The Vienna Experience: Characterizing Acute Lung Allograft Dysfunction (ALAD) In Lung Transplant Recipients

Sophia AUNER[1], Caroline HILLEBRAND[1], Panja M. BOEHM[1], Stefan SCHWARZ[1], Zsofia KOVACS[1], Clemens AIGNER[1], Konrad HOETZENECKER[1], Peter JAKSCH[1], Alberto BENAZZO[1]

[1]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

The term "acute lung allograft dysfunction" (ALAD) is gaining increasing recognition; however, its definition remains debated. The aim of this study was to characterize ALAD patients in a large, single-center cohort, providing a deeper insight into this yet poorly defined type of graft dysfunction.

Methods

Patients undergoing lung transplantation between January 2017 and December 2023 were included. Those with fewer than four pulmonary function tests (PFTs) or under 6 months of follow-up were excluded. ALAD was defined as a $\geq 10\%$ decline in FEV1 within a 12-week period that returned to baseline. If FEV1 failed to recover, patients were classified as having chronic lung allograft dysfunction (CLAD), per the International Society for Heart and Lung Transplantation (ISHLT) criteria.

Results

A total of 647 patients underwent transplantation during the study period. Of these, 40 were excluded due to inadequate follow-up data or insufficient PFTs. 181 (28%) experienced at least one episode of FEV1 drop with subsequent return to baseline during the follow-up period. Of these 181 FEV1 drops, 134 were attributed to identifiable causes contributing to the decline in lung function.

Notably, 47 patients (7%) met the criteria for ALAD, with no other identifiable causes for the decline in lung function and recovery to baseline within three months. The median onset of ALAD was 228 days (IQR 116-421) after transplantation. Interestingly, patients with ALAD had a significantly lower CLAD-free survival (p=0.013) than patients without ALAD, even when compared to patients with a reversible FEV1 drop due to a known cause, such as infection (p=0.019).

Conclusions

ALAD was associated with significantly reduced CLAD-free survival, even in comparison to patients with infections and rejections. These findings emphasize the urgent need for a standardized ALAD definition to improve both clinical management and research, ultimately contributing to improved patient outcomes.

---

15 Years Of EVLP In Vienna – An Overview

Panja M. BOEHM[1], Sophia AUNER[1], Jakob HOMOLA[1], Caroline HILLEBRAND[1], Shahrooz NASROLLAHI-SHIRAZI[1], Alexis SLAMA[1], Stefan SCHWARZ[1], Peter JAKSCH[1], Clemens AIGNER[1], Alberto BENAZZO[1]

[1]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria

Background

Ex-vivo lung perfusion (EVLP) is a valuable tool for assessing marginal donor lungs and addressing logistical challenges in lung transplantation. As one of the largest lung transplant centers in Europe, we began using EVLP in 2010, and hereby present outcomes from the first 15 years of EVLP in Vienna.

Methods

EVLP was performed using a custom-made system or the XPS™ machine by XVIVO, following the Vienna protocol: normothermic, acellular perfusion with Steen solution at a target flow of 40% of cardiac output. Ventilation began at 32°C with volume-targeted pressure-controlled

ventilation (7 mL/kg ideal body weight, FiO_2 0.21, PEEP 7cm H_2O). Hourly oxygen challenges (FiO_2 1.0) were followed by blood gas analysis. Perfusion, pressures, and ventilation parameters were continuously monitored. Lungs were accepted, if ΔpO_2 exceeded 300 mmHg and deflation compliance was good. Post-transplant outcomes - including PGD, ventilation duration, ICU/hospital stay - were analyzed.

Results
131 clinical EVLP procedures were performed for marginal donor lungs with a 60% conversion rate (n=79), with 112 DBD (86%) and 19 DCD (15%) donors. Fifty percent were female (n=66), median donor age was 49 years (IQR 39-59), and median donor pO_2 was 301 mmHg (IQR 228-373).

Among recipients, 54% were female (n=46), and median age 58 years (IQR 50-66). No PGD grade 3 occurred at 72 hours. Median ventilation time was 48 hours (IQR 12-84), ICU stay 8 days (IQR 1-15), and hospital stay 28 days (IQR 16-40). Observation time was 45 months (range 0-171) with 89% overall survival after 12 months. 20 patients (25%) developed CLAD with a median time to CLAD of 49 months.

Conclusions
Our 15-year experience demonstrates that EVLP is a reliable method for safely expanding the donor pool. Recipient outcomes following EVLP-transplanted lungs were comparable to those of conventional transplants, supporting its continued use in clinical practice.

[1]Department of Transfusion Medicine and Cell Therapy, HLA-Laboratory, General Hospital Vienna, Vienna, Austria
[2]Department of Transfusion Medicine and Cell Therapy, Medical University of Vienna, Vienna, Austria

Background
Donor-specific antibodies (DSAs) play a pivotal role in lung allograft rejection, especially in the context of antibody-mediated rejection (AMR) and chronic lung allograft dysfunction (CLAD). While traditionally assessed in peripheral blood, recent methodological developments allow identification of DSAs bound directly to the allograft. These graft-derived DSAs (graft-DSA) can be detected, e.g., transbronchial biopsies. Graft-DSAs may reflect local immune activation more accurately than circulating DSAs and may become biomarkers for early alloimmune injury and subclinical rejection.

Methods
After sample collection, tissue is processed using acid-elution techniques. Supernatants are neutralized and subjected to Luminex-based single antigen bead assays.

Results
We describe analyses of elution experiments of transbronchial biopsies.

Conclusions
Our findings suggest that bronchoscopic graft-DSA can be reliably detected. Their use for personalized immunosuppressive management should be further studied.

59

Graft-Derived Donor-Specific Antibodies In The Lung: A Novel Biomarker For Local Alloimmune Activation

Daniela Koren[1], Daniela Kriks[1], Tanja Mayer[1], Vanessa Spiegl[1], Lisa Sturm[1], Gottfried Fischer[2]

07_Stem Cell Transplantation

60

Real-World Evidence Of BCMA-Directed CAR T Cell Therapy In Austria: Clinical Outcomes And Safety From A Single-Center Retrospective Analysis

Lina Rüsing[1], Julia Cserna[1], Armin Bumberger[1],
Hanna Knaus[1], Margit Mitterbauer[1], Axel Schulenburg[1],
Sophia Oesterreicher[2], Stephanie Winter[2], Nina Worel[2],
Klaus Podar[3,4] Werner Rabitsch[1], Hildegard Greinix[1],
Hermine Agis[5], Maria-Theresa Krauth[5]

[1] Department of Medicine I, Division of Bone Marrow Transplantation,
   Medical University of Vienna, Austria
[2] Department of Transfusion Medicine and Cell Therapy, Medical
   University of Vienna, Austria
[3] Divison of Internal Medicine II, University Hospital Krems, Krems an der
   Donau, Austria
[4] Divison of Molecular Oncology and Hematology, Karl Landsteiner
   University of Health Sciences, Krems an der Donau, Austria
[5] Department of Medicine I, Division of Hematology and
   Hemostaseology, Medical University of Vienna, Austria

Background

BCMA-directed CAR T-cell therapy is highly effective in relapsed/refractory multiple myeloma, with clinical trials reporting response rates >70%. Recent CARTITUDE-1 data show one-third of patients remain progression-free ≥5 years, with a median overall survival of 60 months. However, European real-world data remain limited.

Methods

This retrospective single-center study included all patients treated with BCMA-CAR T-cell therapy at the Medical University of Vienna between 01/2024 and 06/2025. Analyses focused on toxicity, response kinetics, and the CAR-HEMATOTOX score's predictive value.

Results

Thirty-three patients (median age 65) received cilta-cabtagene-autoleucel (n=21) or idecabtagene-vicleucel (n=12) after a median of 4 prior therapy lines; 39% had prior BCMA-targeted therapy.

CRS occurred in 45% (21% ≥grade 2); tocilizumab was given in 12 patients. ICANS (all grade 1) occurred in 15%; late neurotoxicity in 9% (two grade 5 cases).

Seven patients were predicted as high-risk by the CAR-HEMATOTOX score, experiencing lower nadir counts (Hb 7.7 vs. 9.1 g/dL, p=0.06; platelets 55 vs. 69 G/L, p=0.08; WBC 0.35 vs. 0.93 G/L, p=0.059). Grade ≥3 hematologic toxicities included anemia (27%), thrombo-cytopenia (33%), and neutropenia (100%).

Among 25 evaluable patients (data from 8 patients are pending due to ongoing external follow-up), after a median follow-up of 260 days, the overall response rate was 80% (CR; 64%). Median time to first response was 22 days. Median progression-free survival (PFS) and overall survival (OS) have not yet been reached; estimated 1-year PFS and OS were 57% and 77%, respectively. Patients with progression had more prior therapies (median 6 vs. 3; p=0.009). Non-relapse mortality was 6%.

Conclusion

BCMA-directed CAR T-cell therapy induced deep responses in a heavily pretreated cohort. Compared to CARTITUDE-1, our cohort had lower incidences of CRS and ICANS while maintaining comparable efficacy. A substantial proportion of our cohort had prior BCMA-targeted therapy, distinguishing this real-world population from pivotal trials.

Significant Improvement Of Outcome After Allogeneic Hematopoietic Stem Cell Transplantation For AML Over Time

Julia Cserna[1], Lina Rüsing[1], Hanna Knaus[1], Philipp Wohlfarth[1], Axel Schulenburg[1], Armin Bumberger[1], Wolfgang Sperr[2], Margit Mitterbauer[1], Werner Rabitsch[1], Hildegard Greinix[1]

[1]Department of Internal Medicine I, Division of Bone Marrow Transplantation, Medical University of Vienna, Austria
[2]Department of Internal Medicine I, Division of Hematology and Hemostaseology, Medical University of Vienna, Austria

Background

Acute myeloid leukemia (AML) is the main indication for allogeneic hematopoietic stem cell transplantation (HSCT) and the only curative treatment option for many patients. Although outcome of HSCT has improved over the years, relapse of AML is still a challenge.

Methods

We conducted a retrospective single-center analysis of all patients undergoing HSCT for AML between 01/2010 and 12/2024 to assess changes in outcome over the last 15 years. Patients were divided into two groups based on transplant year and use of posttransplant cyclophosphamide (PTCy).

Results

A total of 546 patients (median age: 53 [IQR: 43-61] years, 47% female) received HSCT, 248 (45%) in group 1 and 298 (55%) in group 2. The later included more older patients (median 51 [IQR: 39-59] vs. 55 [IQR: 45-62] years, p<0.001), ELN 2022 adverse risk (47% vs. 25%, p<0,001), patients in first complete remission at HSCT (73% vs. 62%, p=0.0001), and recipients of myeloablative conditioning (96% vs. 47%, p=0.000). Only in group 2 haploidentical donors (19%) and PTCy (25%) were used. Group 2 patients had significantly less acute GvHD (21% vs. 35%, p=0.000), chronic GvHD (15% vs. 28%, p=0.000), CMV reactivation (27% vs. 39%, p=0.003) and relapse (23% vs. 34%, p=0.007). Non-relapse mortality was significantly lower in group 2 (25% vs. 26%, p<0.001). Survival was significantly better in group 2 with an estimated overall survival of 67% vs. 44% (p=0.000) and an estimated GvHD and relapse free survival of 62% vs. 42% (p=0.000) after a median follow-up of 21 and 49 months.

Conclusions

We observed an improvement in HSCT related complications, relapse rates and survival in patients given HSCT in more recent years. The impact of advancements in supportive care, donor selection and PTCy on these results is currently under investigation in multivariate analyses and will be presented at the meeting.

The Impact Of Tacrolimus Levels On Acute GVHD And Transplant Outcomes In Haploidentical Hematopoietic Stem Cell Transplantation: A Retrospective Analysis

Alexander Nikoloudis[1,2], Buxhofer-Ausch V.[1,2], Kunte A.[1], Groiss C.[1], Mair L.[1], Aichinger C.[1], Binder M.[1], Hasengruber P.[1], Kaynak E.[1], Wipplinger D.[1], Milanov R.[1], Strassl I.[1,2], Stiefel O.[1,2], Machherndl-Spandl S.[1,2], Rumpold H.[1,2], Weltermann A.[1,2], Petzer A.[1,2], Clausen J.[1,2]

[1] Ordensklinikum Linz – Elisabethinen, Interne I, Linz, Austria
[2] Johannes Kepler University Linz, Medical Faculty, Linz, Austria

Venetoclax Plus Azacitidine And Donor Lymphocyte Infusion In Relapsed Acute Myeloid Leukemia After Allogeneic Hematopoietic Stem Cell Transplantation

Armin M. Bumberger[1], Lina Rüsing[1], Julia Cserna[1], Hanna Knaus[1], Axel Schulenburg[1], Margit Mitterbauer[1], Hildegard Greinix[1], Werner Rabitsch[1], Peter Valent[1], Wolfgang Sperr[1]

[1]Department of Internal Medicine I, Medical University of Vienna, Austria

Objectives

To evaluate the impact of early tacrolimus (TAC) blood levels on acute graft-versus-host disease (aGVHD) and transplant outcomes in adults undergoing haploidentical hematopoietic stem cell transplantation (haplo-HSCT) with post-transplant cyclophosphamide (PTCy)-based prophylaxis.

Methods

We retrospectively analyzed 161 adults receiving T cell–replete haplo-HSCT with PTCy, TAC, and mycophenolate mofetil. TAC trough levels from weeks 1–2 (w1/2) and weeks 3–4 (w3/4) post-transplant were categorized as "Low" or "High" using a threshold of 10 ng/mL. Outcomes assessed included grade III-IV aGVHD, non-relapse mortality (NRM), relapse, and overall survival (OS). Multivariate analyses controlled for relevant patient and transplant factors.

Results

Higher w1/2 TAC ($\geq$10 ng/mL) in weeks 1–2 had no significant association with aGVHD incidence (35% vs 35%, P = 0.71). Higher TAC levels during weeks 3–4 were associated with a trending decrease cumulative aGVHD III-IV incidence (8% vs 20%; P = 0.09). Multivariate analysis confirmed w3/4 TAC levels as protective against aGVHD III-IV (sub-Hazard Ratio [sHR] = 0.83, 95% CI: 0.70−0.98, P = 0.03) and NRM (sHR = 0.82, 95% CI: 0.71−0.95, P = 0.01), while w1/2 TAC levels had no significant impact on the above outcomes. TAC levels did not significantly impact OS or relapse.

Conclusions

In haplo-HSCT with PTCy-based GVHD prophylaxis, higher TAC levels during weeks 3–4 post-transplant significantly reduced aGVHD III-IV and NRM. Early TAC levels had limited influence, suggesting initial strong immunosuppression by PTCy may overshadow early TAC effects. Optimal management of TAC levels after week two appears crucial; further studies should validate these findings and explore individualized dosing strategies.

Background

Relapse of acute myeloid leukemia (AML) after allogenic hematopoietic stem cell transplantation (allo-HSCT) remains a significant clinical challenge and the survival of such patients is poor. Venetoclax (400mg; day 1 - day 28) plus azacitidine (75 mg/m^2, day 1 - day 7; VenAZA) is an established intermediate dose therapy in patients ineligible for intensive therapy. Recently, VenAZA has been applied in AML recurrence after allo-HSCT.

Methods

We retrospectively analyzed 12 patients (males: n=9; median age: 57.5 years; range: 39-66) with relapsed AML after HSCT who received VenAZA and were scheduled for donor lymphocyte infusion (DLI) between 04/2023 and 06/2025.

Results

Two of the 12 patients had disease progression despite VenAZA. Two patients showed response to VenAZA, but

no donor chimerism could be achieved after 4 and 7 cycles, respectively. They received a second transplant. Eight patients responded to VenAZA and achieved full donor chimerism. In this cohort, DLIs were administered after a median of 2 cycles of VenAZA (range: 2-5). The DLI dose per administration ranged between 1x10^6 - 5x10^7 CD3+ cells/kg (median administrations = 3, range: 2-3). VenAZA was continued for a median of 2 cycles after initiation of DLIs (range 0-3). Reasons for discontinuation were relapse, GvHD and treatment related toxicity in two patients each and patient preference in one case. The two relapsed patients received salvage therapy (FLAG) but had no sustained response. In one patient, VenAZA was deescaleted to hypmethylation only because of treatment related toxicity. Six patients were alive and relapse free in June 2025 (median follow up 15.3 months, range 10.7 - 20.9). The median overall survival of all 12 patients was 13.8 months (range 1.6 - 24.3).

Conclusion

According to our results, the combination of VenAZA with DLIs might be a viable therapy option in patients with relapsed of AML after allo-HSCT.

64

Fludarabine Plus Treosulfan Conditioning For Older And Comorbid Patients Before Allogeneic HSCT - A Retrospective Analysis Of Patients Treated At The Medical University Of Vienna

Hanna Knaus[1], Christina Schüller[1], Lina Ruesing[1], Julia Cserna[1], Margit Mitterbauer[1], Axel Schulenburg[1], Werner Rabitsch[1], Hildegard Greinix[1], Philipp Wohlfarth[1]

[1] Stem Cell Transplantation Unit, Department of Medicine I, Medical University of Vienna, Vienna, Austria

Background

Allogeneic hematopoietic stem cell transplantation (HSCT) with reduced-intensity conditioning (RIC) has expanded treatment options for older and comorbid patients with myeloid malignancies. Fludarabine/treosulfan (Flu/Treo) has demonstrated promising results, including in Beelen et al. (2020), where it was compared to RIC-fludarabine/busulfan (RIC-Flu/Bu). We evaluated Flu/Treo in a cohort from the Medical University of Vienna and compared outcomes to Beelen et al.

Methods

We retrospectively analyzed 62 patients who received Flu/Treo-based HSCT between 2020–2024. Diagnoses were AML (69.3%), MDS (11.3%), and MPN (19.4%). Median age was 63.1 years (range 40–74); HCT-CI was ≥ 2 in 44%. Conditioning included treosulfan 10 g/m^2 (for 3 days) and fludarabine 30 mg/m^2 (for 5 days), as in Beelen et al. Median follow-up was 9.7 months (range 0.3–37). Outcomes - overall survival (OS), relapse, non-relapse mortality (NRM), engraftment, and acute/chronic graft-versus-host disease (GvHD) - were reported with 95% confidence intervals (CI) and compared to Beelen's Flu/Treo and RIC-Flu/Bu cohorts.

Results

One- and two-year overall survival (OS) were 88% (CI 78–98) and 76% (CI 60–96), respectively. Median neutrophil and platelet engraftment occurred on days 16 and 13. Day-28 donor chimerism was complete in 79%. Cumulative relapse at 1 and 2 years was 15% (CI 6.1–26). aGvHD occurred in 31% (CI 19–43), cGvHD in 11% (CI 3.9–23). NRM was 4% at 1 year and 7.8% at 2 years. Compared to Beelen's Flu/Treo cohort, our group had higher 2-year-OS (76% vs. 64%), similar aGvHD (31% vs. 32%), lower cGVHD (11% vs. 18.4%), and faster engraftment. Compared to RIC-Flu/Bu, there was superior 2-year OS (76% vs. 50.4%) and lower NRM (7.8% vs. 19%).

Conclusions

Flu/Treo conditioning yielded favorable survival, low relapse and NRM, and low rates of acute and chronic GvHD. These data support Flu/Treo as a safe, effective RIC regimen for elderly or comorbid HSCT patients.

65

Strengthening Communication In Intensive Care Units To Support Organ Donation In Austria

Laura Hamedl, Benjamin Kölldorfer

Austrian National Public Health Institute, Vienna, Austria

Background

In 2024, Austria registered 311 deceased persons as potential organ donors (34.0 per million people), yet only 166 (18.1 pmp) of these potential organ donors were actually utilized donors. To address the medical requirements of patients on transplant waiting lists, a target value of 30 OSP pmp has been set. A significant challenge arises in communicating with relatives, particularly in the context of disclosing death and organ donation. ÖBIG-Transplant's communication training programme aims to strengthen the communication and social competencies of intensive care staff to foster greater acceptance of organ donation. In 2025, a total of 7 communication seminars can be offered throughout Austria.

Methods

The communication seminars are part of a national support programme for organ donation and transplantation, funded by the Federal Health Agency and implemented by ÖBIG-Transplant. The seminars consist of three distinct formats, each with a specific focus and conducted by a team of professional trainers. The training is based on evidence-informed communication models and includes practical application in simulated scenarios with professional actors, followed by structured reflection sessions.

Results

Over the past 20 years, 2,145 professionals have participated in ÖBIG-Transplant's communication seminars – 61% from nursing, 32% from medicine, 4% from psychology, 2% transplant coordinators, and 1% from other fields. In 2024, 84 people completed the ÖBIG-Transplant communication training. The very positive feedback, as evidenced by 84 anonymous feedback forms and personal comments, validates the efficacy of the support measure.

Conclusions

The communication seminars are a well-established and effective measure to support organ donation in Austria. They are highly valued by healthcare professionals and can make a decisive contribution to increasing donor numbers. Continuous evaluation and adaptation ensure their ongoing relevance in clinical practice.

66

Every Organ Counts: The Role Of Second Opinions In Optimizing Organ Transplantation In Austria

Theresia Unger, Annika Herding, Marianne Ganahl

Gesundheit Österreich GmbH

Background

In times of low organ donor availability, it is especially critical to thoroughly evaluate whether an organ is suitable for transplantation before deciding against reporting the potential donor or specific organs to Eurotransplant due to concerns about organ quality.

Methods

In Austria, a second opinion system was established in 2017 and has since been integrated into the online tool

used for documenting donor protocols. Data from 2024 were analysed to assess the implementation and potential impact of the second opinion process on increasing organ transplant rates. Additionally, regular outcome reviews are conducted for transplants performed after obtaining a second opinion.

Results

The findings indicate that, in most cases, organs are primarily reported to Eurotransplant. When organs are not reported, the designated exclusion reasons outlined in the protocol are usually cited. In some instances, alternative medical justifications are provided for non-reporting. Nonetheless, in 2024, the second opinion process led to the identification of (a small number of) additional transplantable organs. The second opinion process is also partially reviewed during audits of transplant centres.

Conclusions

Obtaining a second opinion is a valuable tool in enabling extended criteria donations. The procedure has become standard practice in Austrian transplant coordination centres. Given the limited number of available donors, each additional organ is vital to ensure timely transplantation for patients on the waiting list. Routine documentation of second opinions ensures the process is consistently followed. When additional organs are transplanted as a result, outcomes are favourable in the majority of cases.