Abstracts of the 2024 CST Annual Scientific Meeting

The CST's annual scientific meeting provides a forum for the transplantation community to share ideas, leading practices, innovative science, and educational content in transplant care. The 2024 CST Annual Scientific Meeting was held at the Westin , Montréal, Québec, October 14-18, 2024. With over 450 Canadian and International delegates attending, the 2024 CST ASM received outstanding educational programming, but also rare opportunities to connect with Transplantation professionals from all over the world.

ID#2

Title: Quality improvement tools to manage organ donation processes: An instrumental case study

Amina Silva - Brock University

Objective: This study aims to analyze a non-conformity in the organ donation process, using a case from South Brazil, and develop a quality improvement tool to control the steps of organ donation, preventing future errors in donor management.

Methods: An exploratory descriptive study of the experience report type was conducted, employing the instrumental case study approach proposed by Robert Yin. Additionally, the Ishikawa diagram and brainstorming technique were utilized to analyze non-compliance in organ donation and propose a quality tool for process improvement.

Results: In a deceased organ donation case, the surgery to extract multiple organs proceeded smoothly. However, communication breakdowns led to inadequate family notification and body preparation, resulting in post-burial complaints. The analysis revealed discrepancies between documented and executed processes, prompting the development of a checklist for organ donation process verification. This checklist, tested in a pilot study and implemented in all donation processes, addresses notification, family communication, clinical assessments, documentation, and body preparation. Despite the irreversibility of the initial error, the study emphasizes the constructive use of quality tools for healthcare process analysis. The checklist addresses critical aspects, including notification protocols, family communication, clinical assessments, accurate documentation, and proper body preparation. The emphasis on communication, responsibility awareness, and effective procedural steps aligns with best practices in healthcare quality management.

Conclusions: The study's outcome, a publicly available quality tool, allows for future implementation studies, assessing the checklist's effectiveness in preventing organ donation process failures in Brazil. Furthermore, the study advocates for a constructive approach to errors in healthcare, steering away from punitive actions that might negatively impact involved parties. The resulting checklist, made publicly available, holds the potential for further implementation studies. This allows for an evaluation of its effectiveness in preventing organ donation process failures, contributing to the enhancement of organ donation practices in Brazil and potentially serving as a valuable model for healthcare improvement worldwide.

ID#3

Title: Compassion Fatigue, Moral Distress, and Burnout Among Organ Donation Coordinators in Canada: Results from a National Mixed-Methods Study

Vanessa Silva e Silva - Brock University

Introduction: Organ donation coordinators (coordinators) play a critical role in organ donation from approaching families for donation to organizing surgical procedures. However, due to the emotionally challenging and stressful scenarios faced daily, coordinators commonly experience work-related issues, such as burnout. Work-related issues among coordinators can lead to increased turnover rates and decreased quality of deceased organ donation processes. Still, little is known about the incidence of work-related issues among coordinators in Canada. Thus, we explored the incidence and potential causes of work-related issues among coordinators in Canada to inform the development of future solutions.

Methods: Mixed-methods study (cross-sectional survey and qualitative interviews). All Canadian coordinators (n=175) were invited to participate in our study. Quantitative data were analyzed using descriptive and inferential statistics (SPSS software) and qualitative data were analyzed using a thematic analysis approach (NVIVO).

Results: 120 coordinators (70% response rate) responded to the survey: 81% were women; 98% were registered nurses and 70% had seriously considered leaving the job at some point in their career. Coordinators presented moderate to high levels of burnout; high levels of moral distress; high compassion satisfaction and secondary traumatic stress; and low resilience levels. Qualitative data mostly supported the quantitative results, but surprisingly, coordinators felt that burnout is part of the role, and contradicting the quantitative findings, that they are very resilient. In addition, coordinators reported as sources of stress the need for structured training and increased organizational support.

Conclusion: This is the first large-scale study to measure work-related issues among coordinators. Canadian coordinators are highly impacted by the stressors and emotional aspects of their job. The results of this work are informing the development of interventions by our research team to help improve the work-related well-being of those professionals, which will consequently reduce turnover rates and increase the quality of deceased organ donation.

ID#4

Title: Donor Audits in Deceased Organ Donation: a scoping review

Amina Silva - Brock University

Background:

Organ transplantation is a cost-effective treatment for organ failure, but a significant gap exists between the number of available organs and the demand for transplants. Donor audits (DA) have been proposed as a tool to identify barriers in the deceased organ donation process and guide quality improvement efforts. However, there is limited comprehensive evidence on the use and impact of DA in clinical settings. Therefore, in this study we sought to collate and summarize existing literature on DA and how they have been used to guide deceased organ donation and transplantation system performance and quality assurance.

Methods:

This scoping review followed the Joanna Briggs Institute (JBI) guidance and PRISMA-ScR reporting standards. We conducted a systematic search of literature on MEDLINE, Cumulative Index of Nursing and Allied Health Literature, and Web of Science supplemented by Google on 6 May 2022. We aimed to search studies published after 1995 in English, French, and Spanish. Eligible studies included those reporting on DA focusing on estimating potential and actual deceased organ donors in various healthcare settings.

Results:

From 2,416 unique citations, 52 studies met the inclusion criteria. The majority focused on estimating potential donors and quantifying actual donors, highlighting missed donation opportunities, with most studies conducted in the UK and published between 2001 and 2006. Motivations for DA included enhancing donation programs and guiding quality improvement efforts. Barriers to donation included family decline and failure to identify potential donors. Quality improvement initiatives suggested including enhancing healthcare professionals' education and improving donor management protocols.

Conclusion:

DA provide valuable insights into deceased organ donation programs and can help identify missed donation opportunities and barriers in clinical settings. Strategies to address these barriers, such as improving family approaches and strengthening donation practices, may enhance access to organ transplants. Further research is needed to assess the efficacy of DA in improving organ donation rates and transplant outcomes.

ID#5

Title: Organ Donation Following Medical Assistance in Dying: A Canadian Environmental Scan

Amina Silva - Brock University

Background: Organ donation following MAiD presents intricate moral and ethical considerations, touching on societal norms, individual autonomy, and donation related experiences for all those involved. While this practice offers potential relief for organ shortages, its novelty demands tailored regulations and guidelines to ensure safety and ethical practice. As Canada leads in this domain, this environmental scan is an initiative from Canadian Blood Services aimed to elucidate the various elements of organ donation processes following MAiD in Canada.

Methods: Multi-phased research approach where phase 1 involves updating a scoping review previously conducted by our research team on organ donation practices following MAiD worldwide. Phase 2 will employ a cross-sectional survey to gather insights from Organ Donation Organizations (ODOs) and healthcare professionals (HCPs) regarding current practices and challenges across Canada. Phase 3 will use a qualitative approach to interview Organ and Tissue Donation Coordinators (OTDCs) and MAiD providers to delve deeper into procedural details and experiences in Canada. Phase 4 will entail a retrospective data review to analyze organ donation statistics of MAiD patients across Canadian ODOs.

Ethics: Research approval is being obtained at Brock University and all phases adhere to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2), including obtaining informed consent and ensuring confidentiality.

Implications and Dissemination: This environmental scan is currently being developed, and our findings will help inform policy change, clinical practice, and educational initiatives surrounding organ donation following MAiD across Canada. Results will be disseminated through peer-reviewed publications, conference presentations, and engagement with relevant stakeholders.

ID#6

Title: Eplet mismatch thresholds: a high-resolution approach for risk assessment and prognosis in renal transplant patients

Ze Chen Wang - University of Saskatchewan

Background

In kidney transplantation, HLA epitope match provides an advantage over conventional antigen match for risk stratification. By analyzing specific epitopes (eplet) recognized by the immune system on the HLA molecules, molecular match allows for a more precise evaluation of immunological compatibility between donor and recipient. This enhances graft survival rates and enables individualized risk assessment, guiding donor selection and transplant management for improved patient outcomes

Methods

Prior research showed eplet mismatch load at HLA-DQ correlates with donor-specific antibody (DSA) formation and graft rejection. Here, we used the Brazilian Eplet registry database and examined the relationship between eplet mismatch and DSA formation at each HLA locus using data collected from 626 patients monitored after renal transplants. High-resolution HLA data was obtained through high-resolution sequencing or prediction based on low-resolution typing through the HaploStats database.

Results

We observed that DSA was most often formed against HLA-DQ (58/499) and saw a wide range of eplet mismatch loads within the study population. We found eplet mismatch cut-offs that were significant for the risk of DSA formation in HLA-A, B, C, and DQ (15, 11, 9, 9, $p < 0.05$). Subsequent Kaplan-Meier survival analysis confirmed these findings and showed a significant difference in DSA-free survival between risk-stratified groups (5%, 3%, 10% at 10 years, $p < 0.05$)

Conclusion

Eplet mismatch thresholds represent a high-resolution method for risk assessment of post-transplant patients compared to traditional antigen mismatch. They can guide clinicians in determining risk and offer patients accurate prognoses. Integrating clinical data and exploring the significance of specific epitopes and eplet mismatches can improve post-transplant management and transform patient care.

ID#7

Title: Ethical issues in normothermic regional perfusion in controlled organ donation after determination of death by circulatory criteria: A scoping review

Nicholas Murphy - Western University

Background: Normothermic regional perfusion (NRP) is a postmortem technique that can improve the quality and number of organs recovered for donation after determination of death by circulatory criteria. Despite its promise, many jurisdictions are reluctant to adopt NRP due to unresolved ethical issues. To inform stakeholders, this scoping review provides an impartial overview of the major ethical controversies surrounding NRP.

Methods: We undertook this review according to a modified 5-step methodology proposed by Arksey and O'Malley and previously used for scoping reviews of bioethics literature. Publications were retrieved through Medline, Embase, and Google Scholar. Unpublished sources and gray literature were sourced from Canadian organ donation organizations, English-language organ donation organization websites, and consultation with our research networks. Three reviewers independently screened all documents against inclusion and inclusion criteria, extracted data, and participated in content analysis. Disagreements were resolved through consensus meetings.

Results: 71 documents substantively engaging with ethical issues in NRP were included for full-text analysis. Document types included position statements, argument-based articles, commentaries, protocols, and reviews. We identified six major themes encompassing a range of ethical debates: (1) NRP's compatibility with the dead donor rule, the injunction that organ recovery cannot cause death; (2) the risk of donor harm posed by NRP; (3) uncertainties regarding consent requirements for NRP; (4) risks to stakeholder trust posed by NRP; (5) NRP's implications for justice; (6) NRP's potential to advance the goals of beneficence by benefiting stakeholders.

Conclusion: We found no consensus on the ethical permissibility of NRP. Despite the polarity of viewpoints, there is agreement that some debates may be resolved through further empirical study. As healthcare providers and other decision-makers nationally and internationally contemplate the adoption of NRP, it is critical they address the ethical issues facing NRP to ensure stakeholder trust in deceased donation and transplantation systems is preserved.

ID#8

Title: Pre-transplant neutrophil-to-lymphocyte ratio and alpha-fetoprotein slope are superior predictors to total tumor volume for hepatocellular carcinoma recurrence after liver transplantation

Ana Jivan - Université de Montreal

Background: Liver transplantation is an established treatment modality for hepatocellular carcinoma (HCC), and accurate prediction of outcomes is essential. Total tumor volume (TTV) is used in many jurisdictions as criteria for patient eligibility. Rising alpha-fetoprotein slope (AFP) and high neutrophil-to-lymphocyte ratio (NLR) have been previously shown to predict outcomes in cancer. This study aims to compare the predictive value in post-transplant HCC recurrence of rising AFP slope, NLR and TTV pre-transplant, and TTV and vascular invasion on explant.

Methods: We reviewed all adult patients who underwent transplant for HCC in a single centre from 1996 to 2020. Natural AFP slope was calculated using data prior to any treatment. NLR was calculated using a median of all available pre-transplant data points, and threshold for high NLR was determined using a ROC curve. Pre-transplant TTV was obtained from imaging around time of listing. Vascular invasion and explant TTV were obtained from explant pathology reports. Data was analyzed in relation to post-transplant recurrence of HCC using multivariate Cox regression.

Results: Our cohort comprised 220 patients: 31 had recurrence (14.1%). Pre-treatment AFP slope of over 1µg/L/day (HR 3.90 [95% CI 1.50-10.17, p < 0 .0054]) was significantly associated with HCC recurrence, as was all-time median NLR above 2.394 (HR 3.77 [95% CI 1.28-11.12, p < 0 .0163]). Pre-transplant TTV as a continuous variable failed to show association with recurrence (OR 0.53 [95% CI 0.24-1.14, p < 0 .1044]). On explant, both vascular invasion and post-explant TTV were found to be strong predictors for recurrence (respectively, HR 4.61 [95% CI 2.23-9.54, p < 0 .0001] and OR 5.74 [95% CI 2.52-13.06, p < 0 .0001]).

Conclusion: Multivariate analysis showed a high pre-transplant NLR and a rising AFP slope were predictive of HCC recurrence after transplant. Pre-transplant TTV failed to predict HCC recurrence in this patient cohort. Our data supports using NLR and AFP slope as adjuncts to pre-transplant decision making.

ID#9

Title: Isolated kidney transplantation in an adolescent on Lumasiran therapy for Primary Hyperoxaluria type 1

Atessa Bahadori - The Hospital for Sick Children

Background: Primary hyperoxaluria type 1 (PH1) is a rare inherited disorder of glyoxylate metabolism resulting in overproduction and deposition of oxalate in end-organs, leading to kidney failure and systemic oxalosis. Liver-kidney transplantation is currently recommended for patients with kidney failure as kidney transplant (KT) alone leads to graft loss due to oxalate deposits. Use of novel small interfering Ribonucleic Acid therapy that knocks down key enzymes involved in hepatic oxalate synthesis (Lumasiran by inhibiting glycolate oxidase) has led to several successful isolated KT, but the experience remains limited. We report our experience with isolated KT in a 13-year-old child with PH1 under Lumasiran therapy. Methods: Case Report. Results: An 11-year-old girl presented with kidney failure and was diagnosed with PH1. She was hemodialysis-dependent and after commencing Lumasiran, plasma oxalate (POx) levels decreased from 83 µmol/L at presentation to stabilize between 40-60 µmol/L, following which she was listed for an isolated deceased-donor KT. At the time of transplantation, POx level was 59 µmol/L. To mitigate risks of oxalate-induced injury to her graft, she was dialysed immediately pre-transplant, as well as post-transplant for oxalate clearance. She had immediate graft function and was started on vitamin B6 and urinary alkalinization therapy. POx levels decreased to 17 µmol/L on post-transplant day (POD) 1 and remained < 25 µmol/L (figure 1). A biopsy on POD18 in the setting of a creatinine nadir around 100 µmol/L showed a small number of tubules with calcium oxalate crystals. At 6 weeks post-transplant, a 24-hour urine collection showed a urinary oxalate level of 2.2 mmol/1.73m2/24h with a POx level of 17 µmol/L. At 8 months post-transplant, she continues to have acceptable allograft function (serum creatinine 93 µmol/L, eGFR 56 ml/min/1.73m2). Conclusion: Our case illustrates the short-term success of isolated kidney transplant in a child with PH1, under Lumasiran therapy.

ID#10

Title: Mind the Gap: Exploring the Mental Health Needs of Cystic Fibrosis Patients Who Undergo Lung Transplantation

Shannon Wright - University Health Network

Background: Adult cystic fibrosis (CF) patients who undergo lung transplant experience an increase in psychological distress in the early post-transplant period. At present, there is limited data to inform how to meet these mental health needs. The aim of this study is to explore the mental health needs of CF lung transplant recipients (CF-LTR) and to inform future patient-centred interventions that are relevant from a patient, caregiver, and healthcare provider (HCP) perspective.

Methods: Mixed methods study using semi-structured interviews and standardized mental health screening tools.

Quantitative Data Collection: CF-LTR participants completed both the Patient Health Questionnaire nine item scale (PHQ-9) and the Generalized Anxiety Disorder seven item scale (GAD-7).

Qualitative Data Collection: Semi-structured interviews with 3 stakeholder groups (CF-LTR < 4 years post-transplant, their caregivers, and HCPs) to explore the lived experience of CF-LTR in the post-transplant period, identify if there are any unmet mental health needs, and explore how these needs could be better addressed.

Results: Twenty-five participants were enrolled, which included six CF-LTR, seven caregivers, and eleven HCP (see tables).

Preliminary results indicate CF-LTR experience psychological distress in the early post-transplant period. CF-LTR and their caregivers identified that access to mental health resources should be a “mandatory” element of their care. HCPs do not routinely screen CF-LTR in the post-transplant period for mental health needs nor do they feel well-equipped to do so. Final analysis of data will reveal future patient-centred interventions that are relevant from a patient and healthcare provider perspective.

Conclusions: This study addresses the current gap in the literature regarding the unique mental health needs of CF patients who undergo lung transplants and the mental health care they receive. The data from this study will inform future patient-centered interventions that may support best practice guidelines in lung transplant programs and transplant mental health programs.

ID#11

Title: Drug repositioning in sIRI models to prevent proinflammatory damages in stored organs

Rabindra BHATTACHARJEE - London Health Sciences Centre

Introduction: Ischemia reperfusion injury (IRI) causes inflammation and cell death in donor kidneys. This leads to poor organ function posttransplant. Therapeutics that prevent such damage, caused by hyperactive Toll-like receptors (TLR) systems, should be helpful in preserving organ quality pretransplant. Therefore, we have developed simulated ischemia reperfusion injury (sIRI) models in human kidney tubular HK cells to facilitate a high-throughput screening of a drug library.

Method: To mimic clinical IRI conditions, HK-2 cells are subjected to hypoxia for 1h at 37°C in a hypoxia chamber, sealed in a bag for 24h at 4°C (anoxia), and reoxygenated at 37°C for 24h. Cell supernatants are tested for injury markers (KIM1, NGAL), TLR ligands (damage associated molecular patterns; DAMPs) and inflammation markers (IL-6, TNF-α etc.) by ELISA. Cell death and viability are also assessed. For drug repurposing, THP1-Blue™ cells are incubated with DAMPs+drug simultaneously for 24h. NF-κB-inducible alkaline phosphatase reporter gene products are measured by Quanti-Blue. Optimization of discarded human kidney perfusion methods are currently underway.

Result: Our results show sIRI condition increases cell death by both necrosis and apoptosis. DAMPs such as HMGB1, which activates the innate immune system through TLRs, and other predominant cytokines, are present in sIRI cell culture supernatants, as indicated by bead-based high throughput Multiplex ELISA assays. Kidneys preserved at 22°C had greater creatinine clearance and urine production compared to 4°C cold storage. Also, ischemia reperfusion injury-induced inflammatory markers were markedly reduced at 22°C compared to 4°C preservation. However, H&E and TUNEL scores may require further modification of evaluation.

Significance: Our model provides the foundation for future research aimed at improving organ preservation. The identification of a drug candidate that can ameliorate the damage from IRI will help optimize current organ preservation conditions.

ID#12

Title: Assessing The Specificity Of The Virtual Cross-Match In Kidney Transplant Patients With Higher Panel Reactive Antibodies: A Call For Modifications Of Our Protocols At A Canadian Tertiary Health Care Institution

Martin Igbokwe - London Health Sciences Centre

Introduction

In our centre, we perform renal transplants according to negative virtual crossmatch (VXM) without the final flow crossmatch for confirmation if there is low likelihood of sensitization or cPRA≤20%. For patients with cPRA>20%, we still await confirmatory flow crossmatch as the false negative flow crossmatch rate in the sensitized population in our centre is unknown. This study is aimed to review the ability of VXM to independently predict negative crossmatch results among patients with different cPRA categories.

Materials and Methodology

This was a retrospective review of all virtual crossmatches performed on potential kidney transplant recipients at a Canadian tertiary health care institution between January 1st 2020 and December 31st 2023. These included primarily assigned renal transplant recipients and in some cases, backup recipients . The cPRA, donor specific antibody (DSA) titre, final T and B cell XM results were also analysed.

Results

Over the 4 years reviewed, 955 patients were analysed. 62% of potential recipients had cPRA≤20, whereas similar numbers of patients had cPRA in the 21-40, 41-60, 61-80 and >81% cPRA ranges(Fig 1). A similar proportion of positive T & B cell crossmatch between the 0-20, 21-40 and 41-69% groups but there was a statistically significant proportion of positive crossmatch in the 61-80 and 81-100 groups (p=0.0001 and 0.0000 respectively)(Table 1). A positive DSA was only statistically significant in the 81-100 category (Table 2).

Conclusion

The likelihood of having a false positive VXM is very low if cPRA ≤60%. Consideration of performing renal transplantation at our centre without prospective flow cross match with a negative VXM should be entertained.

Key words: Kidney transplantation, Virtual cross-match, cumulative panel reactive antibody, deceased donor

ID#13

Title: Evaluating the Impact of a Deceased Donor Workshop on Participant's Skills and Confidence

Prachi Patel - University Health Network

Background

Deceased donor organ recovery is a complex and time-sensitive procedure that is often performed by surgical fellows. However, there are limited formal training opportunities, and no standardized curriculum exists in North America. To address this, we developed a deceased donor workshop and evaluated its effect on participants' confidence, proficiency, and knowledge.

Methods

Thirteen abdominal transplant fellows, five general surgery residents, one attending surgeon and one first-assist nurse attended the workshop. The course was developed by international leaders in transplant surgery and conducted over two days with combination of didactics and hands-on experience with cadaver lab. Pre-and post-survey responses were compared using the Wilcoxon test.

Results

Nineteen responses were included in the analysis after removing incomplete responses. Participants' confidence in conducting deceased donor organ recovery increased significantly after the course (33.3% to 60%, p-value < 0.001), as did their confidence in performing the back table operation (33.3% to 70%, p-value < 0.001). Their confidence improved most in donor pancreas recovery (32.4% to 56.4%, p-value < 0.001). Of all, 84% of participants agreed that they gained new technical knowledge, and 79% expressed feeling safer about performing procedures in the clinical setting.

Conclusion

The deceased donor workshop improved participants' confidence in performing organ retrieval and helped them acquire the skills needed to perform the procedure safely. The deceased donor workshop can be an important tool to supplement current institutional training paradigms and can help standardize organ recovery across North America.

ID#14

Title: Defining Protective And Pathogenic Resident Immune Cells In Kidney Transplantation

Martin Mak - University Health Network

Background: Transplantation is the optimal treatment for end-stage kidney disease, which affects over 40,000 Canadians. Following transplantation, the organ can suffer ischemia reperfusion injury, which is associated with delayed graft function and a 38% increased risk of acute rejection. Notably, the incidence of delayed graft function ranges from 20-50% in recipients of deceased donor kidney, compared to only 4-10% in recipients of living donor kidney. While resident immune cells can contribute to or minimize injury post-transplant, it is not clear how these populations differ between deceased and living donor kidneys, and how they interact with recipient immune cells early post-transplant to contribute to poorer clinical outcomes within deceased donor kidneys.

Methods: In this study, we utilize single cell RNA sequencing on pre-transplant living and deceased donor kidneys to identify interactions that might predispose deceased donors to these observed clinical differences. We also employ fixed RNA profiling to map early post-transplant immune responses using matched pre- and post-transplant biopsies from patients that received a deceased donor kidney allograft and experienced delayed graft function within two weeks.

Results: Pre-transplant, we observe that the deceased donor kidney resident immune landscape is enriched for a macrophage population expressing genes involved in autophagy and ubiquitination, supported by elevated expression of macrophage migration inhibitory factor (MIF) and osteopontin (SPP1). This enrichment remains consistent post-transplant, and following recipient cell infiltration we identify a macrophage population expressing BAFF, CD40, TRAIL, and chemokines CXCL10 and CCL8. Cell-cell interaction analyses predict this population to promote B and T cell proliferation and development through the BAFF-BAFFR axis and the CXCL10-CXCR3 axis respectively.

Conclusion: Collectively, these studies define key immune interactions in deceased donor kidney allografts that could contribute to poorer clinical outcomes in renal transplantation, and aid in defining pathogenic immune-mediated contributions that could be targeted therapeutically.

ID#15

Title: In-Limbo Pre-kidney Transplant Workup: A Quality Assessment/Process Improvement Program

Abdelrahman Elsebaie - Queen's University

Background: Failure to complete a comprehensive pre-kidney transplant workup results in increased dialysis exposure, poorer patient and graft survival, and higher resource demands. As referrals come to transplant centers, patients who are in 'pending activation limbo' are either neglected or detract from new patients' evaluation. Candidates are worked up by our transplant program post-referral rather than by the dialysis programs. We aimed to assess quality metrics in our program, focusing on variability in the duration of pre-transplant workup among different coordinators, processes, and populations.

Methods: This is a retrospective study evaluating the duration and obstacles of the pre-kidney transplant workup of all in-limbo candidates evaluated at our program prior to January 1, 2021. Data will be compared with candidates' workups during a later period when our newer coordinator adopts a more regular chart review to expedite workups.

Results: 112 candidate's files were reviewed by January 1, 2021. 54 (48.2%) candidates were in-limbo [mean age 54.5±10.7 years, female (44.4%), Caucasian (74.1%)], 38 files were closed due to patients' wishes/nonadherence and 20 had expired. By March 1, 2024, 47 (87%) in-limbo candidates received a transplant decision while 7 patients stayed in workup. Median time from assessment to transplant decision was 23.3 (14.3-37.1) months, while time from chart review to transplant decision was 7.7 (3-16) months. Patients still in workup live further away from our center, were assessed once (P 0.035), and have a longer median workup to date 44.6 (42.4-55.7) months. The median time to transplant decision of candidates with more frequent pre-transplant assessments compared with those with less frequent assessments was shorter (20.2 vs 27.1 months, P 0.037). Finally, at the time of transplant decision, 38 (81%) patients were on dialysis (9 on dialysis < 1 year).

Conclusion: Regular chart review and frequent assessments of pre-transplant candidates result in shorter workup and dialysis vintage.

ID#16

Title: Machine learning enabled optimization of perioperative hemodynamics in renal transplantation

Annudesh Liyanage - University of British Columbia

For patients suffering from kidney failure, a transplant is the best option. Because of the limited amount of kidneys available, it is crucial to ensure that they are not rejected: this means avoiding delayed graft function (DGF). It is hypothesized that hemodynamic variables can be manipulated to mitigate DGF risks. Since classical statistics has been unable to characterize this interaction, we turn to machine learning strategies. We developed a multivariate time series model, based on the XCM architecture, that uses perioperative hemodynamic variables to predict DGF events. Our training set consists of systolic and diastolic blood pressure values from donors with neurologically determined death (278 cases) and cardio-circulatory determined death (150 cases). The time course of these procedures were warped such that key time points (anastomosis start, anastomosis end and procedure end) all occurred at the same indices. To minimize variability between runs, we performed a 50-fold bootstrapping method and averaged these results. In terms of model performance, we achieved an AUROC of 0.72 +/- 0.02 and a precision-recall score of 0.55 +/- 0.02. We also obtained a salience plot whose heatmap values indicate the relative importance for predicting transplant outcomes. This showed that the latter half of the pre-anastomosis period was of greatest importance followed by the earlier part of this period and the anastomosis phase itself. The post-anastomosis period had low relative importance. Overall, we have made a functioning model to predict DGF events with time series hemodynamic variables. With a larger training set, we believe that this model can reliably predict DGF events and be extended to provide targets for an anesthesiologist to avoid them. Our salience maps also suggest that the most crucial period for influencing the success of a transplant is the latter half of the pre-anastomosis period.

ID#17

Title: PANoptosis: an Inflammatory Programmed Cell Death in Human Lung Transplants

Yajin Zhao - University Health Network

Background:

Ischemia-reperfusion induced injury (IRI) in lung transplants (LTx) contributes to primary graft dysfunction. Our previous research revealed that inflammation and cell death related genes are upregulated after reperfusion in human LTx. While activation of various programmed cell death (PCD) pathways has been implicated in IRI in animal models, their existence in human LTx remains unknown. This study aims to identify the expression of genes in different PCD types, explore the interrelationships among them, and their relationships with inflammation in human LTx.

Methods:

A bioinformatic analysis was conducted on 54 paired human lung tissue samples collected at the end of cold ischemic time (CIT) and 2 hours post-reperfusion (R2H). We utilized Gene Set Enrichment Analysis (GSEA) to assess the gene sets of six types of PCD. Single-sample GSEA (ssGSEA) was employed to examine the relationship among PCD pathways. The link between PCD and inflammation was evaluated via single-gene GSEA (sgGSEA).

Results:

Genes in Apoptosis and Necroptosis pathways were significantly enriched after reperfusion in human LTx, followed by Pyroptosis, Ferroptosis, and Autophagy. Interestingly, genes related to Cuproptosis was negative enriched (Fig A). Genes related to Apoptosis, Necroptosis, and Pyroptosis were highly correlated with each other, in both CIT (Fig B) and R2H (Fig C) samples. Moreover, these three types of PCD exhibited connections with the expression levels of PANoptosome-related genes (Fig D), indicating PANoptosis. Further analysis demonstrated that IR-induced PANoptosis correlated with genes related to inflammatory responses.

Conclusion:

This study first highlights the expression of genes related to six PCD pathways in human LTx during CIT and R2H. The discovery of PANoptosis suggests that we should search for common biomarkers and therapeutic targets for this inflammatory cell death in human LTx to alleviate IRI and improve clinical outcomes.

ID#18

Title: Weight-Based MMF (Cellcept®) Dosing in Canadian Kidney Transplant Patients: Quality Improvement Pilot.

Aidan Gangji - Queen's University

Background: Mycophenolate mofetil (MMF) reduces the risk of acute rejection (AR) in kidney transplant recipients (KTRs) and improves post-transplant graft survival. MMF is usually prescribed in fixed doses (2 gm/day). Due to its side effects, MMF doses often require reduction. Weight-based MMF dosing (10-16 mg/kg/day) was correlated with therapeutic level in Asian KTRs. We are aiming to evaluate the safety and efficacy of weight-based MMF dosing at 15 mg/kg/day, adopted by our program in September 2021.

Methods: This is a snapshot study which is a part of a single center retrospective quality improvement pilot study evaluating the safety and efficacy of weight-based MMF dosing at 15 mg/kg/day, compared with non-weight-based doses (≤ 2 gm/day), to reduce the risk of MMF-associated side effects including leukopenia (WBC ≤ 3.5), BK- and/or CMV-viremia, while monitoring the risk of AR associated with reduced MMF doses. All KTRs followed in our kidney transplant clinic at Queen's University between September 1, 2021, and August 31, 2023, were included.

Results: 230 KTRs [Age 56.9±14.4 years, Female (36.1%), Caucasian (87.8%)] were included. By August 31, 2023, 112 (48.7%) patients were on MMF. 18 patients were on weight-based doses (15.9 (14.9-18.1) mg/kg/day). 17 patients were on fixed doses (20.7 (17.2-26.2) mg/kg/day). 34% of MMF patients were on reduced doses (14.4 (10.4-14.4) mg/kg/day) due to adverse effects, most notably leukopenia (25%) and leukopenia (18%). At the end of the study, leukopenia, BK- and CMV-viremia were active in 4 (1.7%), 7 (3%) and 1 (0.4%) of all patients, respectively and none of them were on weight-based doses.

Conclusion: Snapshot data showed a low rate of leukopenia, BK- and CMV-viremia/infection, likely due to effective MMF dose reduction. Further analysis to be done through our next retrospective cohort study to evaluate the outcomes of weight-based dosing.

ID#19

Title: High dose intramuscular influenza vaccine in solid organ transplant patients. A systematic review and meta-analysis

MohammadReza Rahimi Shahmirzadi - Western University

Background: Seasonal influenza can cause serious illness and even death, especially in immunocompromised people such as solid organ transplant recipients (SOT). Early results from some studies show that high dose (HD) intramuscular (IM) vaccine might help boost the body's immune response in transplant patients (1-5). Given the uncertain benefits and harms associated with various IM vaccine doses a synthetized appraisal of the evidence is warranted.

Methods: Randomized controlled trials of adults who underwent SOT and received IM influenza vaccine and compared , IM influenza HD vaccine with standard dose.

The outcomes of interests are seroconversion rate (SCR) for H1N1,H3N2, and graft rejection after vaccination.

We searched MEDLINE, Embase, and Cochrane CENTRAL until Jan 2024.

Screening, data extraction, risk of bias and certainty of evidence assessment were assessed by two reviewers.

Results: Pooling data from the 5 studies (1281 patients) shows moderate quality of evidence in the SCR towards using HD influenza vaccine in H1N1 type and high-quality evidence for H3N2 type . (RR 1.87 (1.25 to 2.79), RR 1.54 [1.31 to 1.80])

Analysis of five studies indicated that HD influenza vaccine results in no difference in graft rejection. (RR 0.73 [0.37 to 1.45]).

High quality evidence showed that HD influenza vaccine reduce serious adverse events in SOT patients. (RR 0.71 [0.52 to 0.96]).

Data from three studies shows HD influenza vaccine may results in little to no difference in confirmed clinically influenza. (low certainty of evidence) (RR 1.16 [0.58 to 2.29])

Conclusion: Our systematic review indicates that HD influenza vaccine probably increases SCR in H1N1 and increases SCR in H3N2.HD vaccine, also may not increase graft rejection and reduces serious adverse events in SOT patients.

ID#21

Title: Dual organ living donation: Canadian single-centre experience of 16 sequential liver and kidney living donors

Anand Ghanekar - University Health Network

Background: Living donors are a critical source of organs for transplantation. With increasing anonymous donation, more are seeking both kidney and liver donation and will travel across Canada for this. Global experience with dual organ living donation is sparse and consensus is needed regarding management of these individuals. We report our Canadian single-centre experience. Methods: Retrospective chart review. Results: 16 sequential dual organ living donors were identified (75% female). Many were motivated by traditional and social media. 4 donors traveled from other provinces for anonymous liver donation. Age at first and second donations was 38.8±11.6 and 41.0±11.5 years. Interval between donations was 2.2±2.2 years. 9 donated both organs anonymously, 5 donated one anonymously, 2 directed both. 69% of first donations and 75% of second donations were anonymous. All hepatectomies were performed via upper midline incision including 10 left lateral segment, 3 right lobe, and 3 left lobe resections. In 8 donors that underwent hepatectomy first, 6 subsequently had laparoscopic left nephrectomy. Open technique was used for 1 right and 1 left nephrectomy due to suspected adhesions from prior ipsilateral hepatectomy. In 8 donors who underwent nephrectomy first (7 left, 1 right), open hepatectomy technique was not altered. Liver donation did not adversely affect renal function in prior kidney donors. Length of stay after second donation was not affected by prior donation. No donors experienced complications. 8 donors participated in kidney paired donation, amplifying their gifts. Conclusions: Dual organ living donation is rare but highly impactful. Anonymous donation plays a major role. Laparoscopic nephrectomy is usually possible following open hepatic resection. Prior organ donation does not affect recovery after second donation. Sequential dual organ living donation can be performed safely whether kidney or liver is donated first. Pan-Canadian consensus on management of these highly motivated individuals may expand the donor pool.

ID#22

Title: Exploring the experiences that enable access to care of post-traumatic stress in pediatric solid organ transplant recipients

Mallorie Tam - University of British Columbia

Background

Many children and adolescents who undergo solid organ transplants (SOT) develop post-traumatic stress (PTS) symptoms. Despite its prevalence and strong association with long-term impairments in quality of life, PTS is often overlooked as a major co-morbidity in many transplant programs. To address this unmet need, the purpose of this study was to explore the factors that impede or facilitate awareness of PTS, access to resources, and readiness to engage with mental health services.

Methods

Separate semi-structured interviews (N=17) were conducted with pediatric SOT recipients between the ages of 12 and 18, and a parent. The interviews explored: 1) awareness and management of PTS symptoms; 2) timelines surrounding PTS symptom awareness and resource-seeking; 3) facilitators to PTS symptom awareness; 4) barriers to PTS symptom awareness; 5) information seeking; and 6) areas for improvement in the current content and availability of resources.

Results

Emotional and physical impacts of SOT were identified for pediatric SOT recipients and their parents. Pediatric SOT recipients experienced lifestyle and social changes around school, friendships, and extracurricular activities. Majority of parent and child/adolescent participants preferred to learn about the risk of PTS and resources to support PTS before the transplant and emphasized that the age of the SOT recipient played an important role related to the timing and content of information shared. The ideal format and source of PTS information were also discussed. Participants recommended several improvements and additional resources to support PTS around access to mental health support, the health care process, counselling and therapy needs, patient-centered support, format, and advocacy.

Conclusions

By exploring the personal experiences and perspectives of pediatric SOT recipients and their parents, this work can be used to improve the accessibility and quality of PTS supports.

ID#23

Title: Challenges and considerations for pre-emptive pharmacogenomic guided voriconazole prescribing in lung transplant recipients

Cindy Luo - Vancouver General Hospital

Background:

Voriconazole undergoes metabolism via CYP2C19, a polymorphic enzyme that results in differences in metabolic activity. Patients with CYP2C19 ultrarapid metabolizer and rapid metabolizer phenotypes are less likely to achieve therapeutic voriconazole levels, which is predictive of treatment failure. Pre-emptive pharmacogenomic testing to determine CYP2C19 variations can help tailor voriconazole therapy for lung transplant recipients.

Methods:

A prospective cohort study has been designed for pre-lung transplant recipients followed at our center. Participants with ultrarapid or rapid metabolizer phenotypes will receive pharmacogenomic guided interventional dosing.

Results:

Despite demonstrating feasibility in a retrospective cohort study of lung transplant recipients at our center, pre-emptive pharmacogenomic testing and use of interventional dosing has revealed multiple unforeseen challenges. Noted issues include additional applications to governing bodies for approval of interventional dosing, test administration workflows, and patient consent.

Conclusion:

Pre-emptive pharmacogenomic testing and interventional dosing for voriconazole poses multiple challenges. Future studies employing similar study design will benefit from early evaluation of workflows. Regulatory changes should be considered to help facilitate implementation of pharmacogenomics to clinical practice.

ID#24

Title: Long-term Outcomes of Kidney Transplant Recipients from Deceased Donors with Circulatory Determination of Death

Lawrence Slapcoff - McGill University

Background: Increased kidney transplantation from donors with circulatory determination of death (DCD) has potential to increase the donor pool; however, concerns remain regarding long-term outcomes associated with their use. Our aim was to evaluate outcomes of kidney transplant (KTx) from brain death donors (DBD) vs. DCD.

Methods: We studied adult KTx recipients from deceased donors from Sept 2011 to Sept 2022. Patients were classified into four subgroups: DBD-SCD (standard criteria donors), DBD-ECD (expanded criteria donors), DCD non-ECD, and DCD-ECD. The primary outcome was death censored graft survival (DCGS). Secondary outcomes included: Primary non-function (PNF), delayed graft function (DGF), death with graft function (DWGF), incidence of first acute rejection and estimated glomerular filtration rate (eGFR).

Results: We included 940 patients, 757 (80.4%) with KTx from DBD and 183 (19.6%) from DCD. 65.2% were male. Among the DBD kidneys, 48.7% were from SCD and 51.3% from ECD. Among the DCD kidneys, 62.3% were from non-ECD and 37.7% from ECD. Immunosuppression consisted of alemtuzumab induction and maintenance tacrolimus and mycophenolate sodium. Prednisone was used in highly sensitized patients. At 10 years, DCGS was: DBD-SCD: 78.8%, DBD-ECD: 70.2%, DCD non-ECD: 80.4%, DCD-ECD: 69.8% ($p < 0.01$). The incidence of PNF was: DBD-SCD: 1.63%, DBD-ECD: 4.38%, DCD non-ECD: 3.51%, DCD-ECD: 5.8% ($p=0.11$). The incidence of DGF was: DBD-SCD: 22.8%, DBD-ECD: 23.2%, DCD non-ECD: 45.6%, DCD-ECD: 44.9% ($p < 0.01$). DWGF at 10 years was: DBD-SCD: 21.5% DBD-ECD: 48.8%, DCD non-ECD: 11.6%, DCD-ECD: 34.6% ($p < 0.01$). The incidence of acute rejection at 1 year was: DBD-SCD: 8.5%, DBD-ECD: 15.4%, DCD non-ECD: 14.2%, DCD-ECD: 10.7% ($p=0.09$). Median eGFR at 1, 5 and 10 years was: DBD-SCD (60, 55, 43), DCD-ECD (40, 35, 22), DCD non-ECD (53, 59, 53), DBD-ECD (41, 38, 44) (1-year: $p < 0.01$, 5-years: $p < 0.01$, and 10-years: $p=0.23$)

Conclusion: DCD remains a critical source of transplantable kidneys. Our findings contribute long-term data supporting their use.

ID#25

Title: Adrenal Insufficiency in Pediatric Kidney Transplantation Recipients

Hyunwoong Harry Chae - University of British Columbia

Background: Immunosuppression of pediatric kidney transplant (PKT) recipients often includes corticosteroids. Prolonged corticosteroid exposure has been associated with secondary adrenal insufficiency (AI); however, little is known about its impact on PKT recipients.

Methods: This was a retrospective cohort review of PKT recipients to evaluate AI prevalence, risk factors and adverse effects. AI risk was assessed using morning cortisol (MC) and diagnosis confirmed by an ACTH stimulation test. Potential risk factors and adverse effects were tested for associations with MC levels and AI diagnosis.

Results: Fifty-one patients (60.8% male, age 7.4 (IQR 3.8, 13.1) years; 1 patient counted twice for repeat transplant) were included. Patients at risk for AI (MC < 2 40 nmol/L) underwent definitive ACTH stimulation testing, confirming AI in 13/51 (25.5%) patients. Identified risk factors for AI included current prednisone dosage (p=0.001), 6-month prednisone exposure (p=0.02), daily prednisone administration (p=0.002), and rejection episodes since transplant (p=0.001). MC level (2.5 years (IQR 1.1, 5.1) post-transplant) was associated with current prednisone dosage (p < 0 .001), 6-month prednisone exposure (p=0.001), daily prednisone administration (p=0.006), rejection episodes since transplant (p=0.003), greater number of medications (beta= -16.3, p < 0 .001), 6-month hospitalization days (beta= -3.3, p=0.013), creatinine variability (beta= -2.4, p=0.025), and occurrence of acute kidney injury (beta= -70.6, p=0.01).

Conclusion: Greater corticosteroid exposure was associated with a lower MC level and confirmatory diagnosis of AI noted with an ACTH stimulation test. Adverse clinical findings with AI included greater medical complexity and kidney function lability. These data support systematic clinical surveillance for AI in PKT recipients treated with corticosteroids.

ID#26

Title: Elements of Expedited Pre-kidney Transplant Workup: A Quality Assessment/Process Improvement Program

Abdelrahman Elsebaie - Queen's University

Background: Failure to complete a comprehensive pre-kidney transplant workup results in increased dialysis exposure, poorer post-transplant patient and graft survival, and higher resource demands. Candidates are worked up by our transplant program post-referral rather than by their dialysis programs. We aimed to assess quality metrics at our program, focusing on variability in the duration of pre-transplant workup after adopting a more frequent and scheduled chart review process by our newer coordinator to expedite pre-transplant workup.

Methods: This is a retrospective study evaluating the duration and obstacles of pre-kidney transplant workup of all candidates, evaluated at our transplant program between January 1, 2021, and December 31, 2022, after adopting a more regular chart review process by our coordinator, with a follow up until March 1, 2024. Data were also compared with historical candidates' workup evaluated at our program prior to January 1, 2021.

Results: 101 candidate's files were reviewed [Mean age 55.4±13.1 years, female (42.6%), Caucasian (76.2%)]. By March 1, 2024, 86.1% of candidates were on dialysis, with 79.3% of those on dialysis by the time of assessment. 78 (77.2%) candidates received a transplant decision while 23 patients stayed in the workup, including 5 candidates who were referred, after completing their workup, to another center for combined organ transplantation. Median time from assessment to transplant decision was 12.8 (7.2-20.4) months, compared with historical candidates' workup of 23.3 (14.3-37.1) months (P < 0 .001). At the time of transplant decision, 64 (63.4%) patients were on dialysis (12 on dialysis < 1 year). Median time from dialysis to transplant decision was 24.1 (12.3-43.2) months, compared with historical candidates' time of 31.6 (5.9-52.4) months (P 0.89).

Conclusion: Frequent and scheduled chart review of pre-transplant candidates results in shorter workup and dialysis vintage.

ID#27

Title: Defining the liver immune microenvironment of Indeterminate Pediatric Acute Liver Failure with single-cell transcriptomics

Harry Sutton - University of Toronto

Background: Indeterminate pediatric acute liver failure (IPALF) is the given etiology in approximately one-third of children who develop ALF. Although termed “indeterminate” recent research using immunohistochemistry (IHC) and bulk RNA sequencing (RNA-seq) suggests many of these patients share a common immune mediated disease.

Methods: Single-cell RNA-seq and fixed RNA profiling was used to define the cellular composition of IPALF livers. IPALF transcriptomic profiles were compared to those made from Wilson’s disease (WD) – ALF, autoimmune hepatitis (AIH) – ALF and healthy pediatric livers. IHC staining was performed to validate transcriptomic findings.

Results: Ex-planted IPALF livers (3 patients, 18,534 cells) contained 16 unique cell types, including nine immune cell subtypes (Figure 1 and 2) . The T cell population was comprised of predominately CD8+ T cells, including one cluster with high expression of granzyme B. Both Granzyme B and CD8 staining were increased in IPALF livers compared to non-IPALF and healthy controls. CCL5 was found to be highly expressed in our T cell population, and inferred ligand-receptor interactions identified CCL5 as interacting with every immune cell subtype. T cell receptor sequencing from one patient with IPALF identified a hyperexpanded clonal population (figure 3) which expressed CD4, CD28 and CD40 as well as CTLA4.

Conclusions: We present the first single-cell analysis of the liver immune microenvironment in IPALF. We confirmed a CD8+ T cell rich environment with high expression of granzyme B in one subcluster. IHC staining for CD8 and granzyme B showed increased staining for both in IPALF livers compared with WD, AIH and healthy controls. CCL5 was identified as highly expressed in IPALF T cells and appears to interact with every other immune subtype. CCL5 may be a rational therapeutic target in the treatment of IPALF.

ID#28

Title: Clinical management and disease burden of cytomegalovirus (CMV) in D+/R- kidney transplant recipients in Canada

Paul Keown - University of British Columbia

Purpose: To document current prophylactic practices, patterns of infection, and disease burden to inform personalized medicine strategies for CMV management.

Methods: A retrospective sequential cohort of 311 CMV D+/R- kidney recipients was enrolled from 7 Canadian programs over 4 years (2018-2021) to define demographic, clinical, therapeutic and health resource use data during the 1st year post-transplant.

Results: Mean age was 52±14 yr., 69% were male and 53% were Caucasian. Diabetes was the principal cause of renal failure (19%); 208 (69%) received a deceased donor (DD) graft; 76 (24%) had ATG induction and 84% had maintenance therapy with tacrolimus and MMF ± prednisone. All received antiviral prophylaxis principally with valganciclovir (90%) for a median 180 days. 106 (34%) patients developed CMV viremia (median peak viral load 14,224 IU/ml) at a median of 218 days of whom 46 (43%) had CMV disease (syndrome or end-organ disease); 15 (14%) had recurrent viremia. Myelotoxicity (neutropenia, leukopenia, pan-cytopenia) occurred in 121 (39%) patients at a median of 88 days and lasted a median of 30 days, with 14 (5%) having >1 episode. Immunosuppression was decreased or discontinued in 108 (80%) episodes and G-CSF added in 23 (19%). Opportunistic infection occurred in 119 patients (38%) at a median of 53 days due to bacterial (48%), fungal (20%) or other viral causes; 30 (25%) had recurrent infections. 141 (45%) patients were hospitalized, 50 (16%) more than once, 25 (8%) for myelotoxicity. 20 patients (6%) had biopsy-confirmed rejection (median 107 days) and 293 (94%) were alive with a functioning graft at 1 year.

Conclusion: Current prophylaxis strategies fail to prevent CMV infection in 34% of high-risk patients. Myelotoxicity, opportunistic infection, reduced immunosuppression and hospitalization remain common and serious complications. More effective and less toxic personalized treatment strategies are required to minimize these risks and burden.

ID#29

Title: HLA Class, Calcineurin Inhibitor Levels, and the Risk of Graft Failure in Kidney Recipients with De Novo Anti-HLA DSA

Sacha De Serres - CHU de Québec

Background: de novo DSA (dnDSA) development is associated with poor outcomes in kidney transplant recipients. However, whether this observation applies to both HLA class I and II dnSDA remains unclear.

Methods: We analyzed a cohort of 1236 consecutive patients who underwent kidney transplantation between January 2000 and December 2021. Anti-HLA antibody screening was performed at 0, 1, 3, 6, and 12 monhts, and then annually posttransplant, as part of the routine surveillance protocol.

Results: During the screening period, 55/1236 (4.4%) patients developed dnDSA prior to graft loss: 18 (33%) to HLA class I only, 22 (60%) to HLA class II only, and 4 (7%) to HLA of both classes. During the follow-up, 30 patients experienced graft loss at a median of 39 months (IQR 10-59) after dnDSA detection: 9/18 (50% HLA class I only, 17/33 (52%) HLA class II only, and 4/4 (100%) HLA of both classes (Fig. 1A). A control group was created by matching patients with dnDSA at a 1:1 ratio to patients who did not develop DSA and had a functioning graft at the time of dnDSA detection in their respective case (Fig. 1B). Compared with these controls, the risk estimates of graft loss were similar between patients with HLA class I only and class II only dsDSA (aHR 2.7, 95% CI 1.1 - 6.6; p=0.04, and aHR 3.1, 95% CI 1.5 -6.6; p < 0 .01, respectively). Additionally, the risk of graft loss decreased with higher calcineurin inhibitor trough levels following dnDSA detection (aHR 0.7 per increase in 1ng/mL; 95%CI 0.6-0.9; p=0.02).

Conclusion: The prognosis of patients with dnDSA seems similar regardless of the HLA class specificity. Lower calcineurin inhibitor levels predict graft loss in such patients.

ID#30

Title: The risk of kidney transplant graft loss in sensitized versus unsensitized patients is modified by prior transplant status

Amanda Nicholson - Dalhousie Faculty of Medicine

Background: Higher panel reactive antibody (PRA) levels increase the risk of kidney allograft loss. Prior kidney transplant (KT) increases the risk of sensitization, however many patients with prior KT remain unsensitized. The aim of this study was to examine the relative risk of adverse events post-transplant associated with increased sensitization versus prior KT status.

Methods: We examined adult patients across the US from 2000-2017 (identified using the SRTR) who underwent a first or second KT. The combined exposure of sensitization status (PRA 0%, >0-80%, and >80%) and prior transplant status (yes, no) was examined using a nested variable with 6 categories. We used propensity score matching (PSM) to create comparable populations between those with a first and repeat transplant. In this matched population, we use multivariable cox proportional hazards models to examine the association between our nested exposure of prior transplant-PRA status and time to death-censored graft loss (DCGL), and multivariable logistic regression to examine odds of delayed graft function (DGF). We examined for effect modification between PRA status (dichotomized at 20%) and prior KT status.

Results: After PSM, 43,366 patients were included in the study (21,683 with prior KT; 21,683 with first KT). There was increased risk for both DCGL (aHR 1.55, 95% CI 1.45-1.65) and DGF (aOR 1.91, 95% CI 1.77-2.07) for those with a prior KT and PRA >80% (relative to no prior KT and 0% PRA), Figures 1a & b. The risk associated with increased PRA was greater in those with a prior transplant. Prior KT modified the known risk of increased PRA associated with both DCGL and DGF (p-value 80%.

ID#31

Title: Patient and caregiver perceptions on the allocation process and waitlist, and accepting a less than ideal kidney: A Canadian Survey

Holly Mansell - University of Saskatchewan

Background: Transplanting less than ideal (LTI) kidneys (e.g., expanded donor criteria, extended criteria, or marginal kidneys) is a strategy for optimizing organ utilization, but little is known about how patients and caregivers perceive the allocation process and waitlist, or LTI kidneys.

Methods: A bilingual anonymous electronic national survey was distributed between January and March 2024. Adult transplant recipients, candidates, and caregivers were recruited through social media posts by transplant organizations and through the Centre hospitalier de l'Université de Montréal (CHUM) and the Saskatchewan Transplant Program. The questionnaire contained sections on demographics, perceptions of organ allocation and acceptance, less-than-ideal kidneys, and educational preferences. A 5-point Likert scale assessed agreement with questions pertaining to organ allocation and decision making when a deceased donor kidney is offered. Descriptive statistics were used to analyze results.

Results: Two hundred fifty-one participants including patients (n=157, 63%) and caregivers (n=94, 38%) from 11 provinces and territories responded, with 54% completing the survey in French. Seventy-four percent (n=186) and 64.5% (n=162) agreed they understood the process of patient placement on the waitlist and deceased-donor kidneys allocation, respectively, but correspondingly 72% (n=181) and 68% (n=171) wanted more information about each. One-third (32%) of respondents felt the waitlist and allocation processes in their province were not transparent. Awareness of the option to refuse a deceased-donor kidney offer was high (n=174,69%), yet nearly half of respondents (n=115,46%) expressed concern about being disadvantaged or removed from the waiting list if they refused a deceased donor kidney offer. Less than a quarter of participants (n= 55,22%) were open to accepting a less-than-ideal kidney.

Conclusions: Enhanced communication is required to improve transparency and information sharing about the allocation system and waitlist in Canada. An educational strategy will be necessary for promoting shared decision making and increasing utilization of LTI kidneys.

ID#32

Title: TNF-a Production by CD14+CD16+ Monocytes Stimulated With EBV synthetic peptides Predicts Long-term and Life-Threatening Over-Immunosuppression Events in Kidney Transplant Recipients

Olivier Désy - CRCHU-Université Laval

Background: Infection and cancer are major causes of premature death in organ recipients. Nonetheless, there has been little advances to personalize immunosuppression. We previously reported that a cell-based assay, measuring CD14+16+TNFa+ monocytes following peripheral blood mononuclear cells (PBMC) incubation with EBV peptides, has high sensitivity to detect over-immunosuppression events in kidney recipients on the short-term. We aimed to develop a risk score prediction for long-term events.

Methods: We studied 551 PBMC samples from 118 kidney recipients followed prospectively over a median of 6.3 years [25th–75th percentiles 3.7–8.3]. PBMCs were cultured overnight, stained and analyzed by flow cytometry. OIS events were defined by the following diagnoses: opportunistic infection, recurring bacterial infections, or de novo cancer.

Results: 40 (34%) patients experienced an over-immunosuppression event: 26 infectious, 11 neoplastic and 3 both. Compared to controls, cases were older and had a shorter time posttransplant. WBC counts and immunosuppression were similar. The mean percentage of CD14+16+TNFa+ monocytes was lower in cases than control (61±18 vs. 71±16%, p

ID#33

Title: Remote patient monitoring of spirometry, oximetry, activity and symptoms in lung transplant candidates with interstitial lung disease

Lisa Wickerson - University Health Network

Background: Monitoring the clinical course of interstitial lung disease (ILD) is essential for recognizing ILD progression and decision-making around further assessment and treatment, including the urgency of lung transplant (LTx). Integrating remote monitoring tools into clinical workflows may optimize clinical management.

Methods: People with ILD listed for LTx were approached after initiation of outpatient pre-habilitation. Participants were given a MIR Spirobank Smart spirometer, Garmin Vivofit 4 fitness tracker and ToronTek G64 pulse oximeter to measure weekly lung function (FEV1, FVC, FEV1/FVC, FEF25-75), daily steps and oxygen saturation after home walking exercise respectively. These biometrics were manually entered into a custom-designed module located within the electronic medical record patient portal (EpicTM) with results integrated into the clinical workflow for clinicians to view. Adherence was defined as reporting weekly entries at least 50% of the time while enrolled. Self-reported health status using the King's Brief ILD questionnaire (KBILD) was entered monthly.

Results: Between October 15, 2023 and April 15, 2024, 26 people were approached and 21 (81%) were enrolled between 2-24 weeks (12 males, 57% with IPF, 61±8 years of age, transplant listing 6-minute walk distance 368±108m, FVC 48±14% predicted, exertional fractional of inspired oxygen 0.46±11, initial median KBILD total score 44.5 (IQR 7)). Reporting adherence was 60% with spirometry, 67% with oximetry and 51% with activity tracking. The limitations noted for lower adherence included challenges in comprehending the spirometer App or task, as well as missed entries due to healthcare appointments or admissions.

Conclusion: LTx candidates were receptive and accepting towards remote biometric monitoring. Future improvements include integration of Bluetooth-enabled tools to improve data collection. The biometrics collected will also inform future work in early detection of deterioration on the transplant waiting list.

ID#34

Title: Testing the feasibility of a mobile application for remote patient monitoring in prospective kidney transplant recipients

Lucas Rempel - University of British Columbia

Background: An accelerated transition from in-person to virtual care has been prompted by both technological advancements and the COVID-19 pandemic. The optimization of mobile support tools is necessary to maintain comprehensive patient care. Kidney transplant (KT) recipients need frequent monitoring given high levels of functional decline and frailty. We have developed a mobile application to facilitate remote patient monitoring among prospective KT recipients.

Methods: We conducted a pilot study testing the accuracy of a mobile application compared to observer assessment for three validated physical function assessment tools: 30-Second-Sit-to-Stand (STS), 6-Minute-Walk-Test (6MWT), and Timed-Up-and-Go (TUG) (Image 1). Following testing, a User Experience Questionnaire (UEQ) was administered. Results are summarized as means ± standard deviation. Comparison between measurements was made using paired t-test and agreement with Lin's concordance correlation coefficient (ccc) and visualized with Bland-Altman Plots (Image 2).

Results: We enrolled 24 participants (N=13 female, N=11 male), with a mean age of 59.6 ± 11.3 years. Participants were predominantly on hemodialysis (75.0%). 18 participants completed the full baseline physical functioning assessment (N=22 STS; N=20 6MWT; N=21 TUG). Compared to observer assessment, the application reliably measured STS (10.0 ± 2.6 vs 9.1 ± 2.9; p=0.057; ccc=0.94) and 6MWT (350.9 meters ± 125.6 vs 365.5 meters ± 118.4; p=0.25; ccc=0.71), but overestimated TUG (10.6 seconds ± 3.6 vs 11.5 seconds ± 2.9; p=0.008; ccc=0.66). 22 participants completed the UEQ, rating the app positively for the following dimensions: attractiveness, perspicuity, efficiency, dependability, and stimulation (Image 3).

Conclusion: This pilot study highlights the feasibility and accuracy of a mobile application used to remotely assess physical functioning in KT recipients. Following additional testing, this application will serve as a valuable support tool to monitor physical functioning, frailty, and follow-up in KT patients.

ID#35

Title: Social media as a tool to explore mental health in pediatric solid organ transplant recipients and their families

Irene Chen - University of British Columbia

Background:

Solid-organ transplantation (SOT) can save a child from organ failure, but it comes with many challenges. Recent studies show higher rates of anxiety, depression, chronic stress, and post-traumatic stress symptoms in pediatric SOT recipients and their families.

While social media serves as an important resource for children and adolescents with chronic health conditions, there is limited understanding of how pediatric SOT recipients, and their families use social media to share and access information. The objective of this project is to determine how the SOT patient community engages in discussions about mental health through social media.

Methods:

A comprehensive search of relevant posts was performed on Reddit (n=2 subreddits) and Facebook (n=22 groups). Publicly available posts containing a self-disclosure as someone or the family member of someone that has received a SOT during 0-24 years of age were retrieved for analysis using inductive content and thematic analysis. We will further code posts using a mental health-specific coding guide. Descriptive statistics will be used to describe the sample.

Results:

Preliminary content analysis of n=50 Reddit posts identified primary codes, including personal experiences pre- and post-transplant, and seeking or providing advice, information, or support. Mental health discussions primarily centered on experiences with medical trauma or depression, as well as attitudes toward death and mental health services in transplant care (see Table 1). Users frequently sought advice on how to cope with mental health or emotional challenges, and group members often offered support in the form of well-wishes, providing reassurance, or validating experiences.

Conclusions:

This study will contribute new evidence and actionable findings on the mental health challenges shared by pediatric transplant patients and their families on social media. By understanding how this community uses social media, we can advocate for the improved quality and availability of mental health resources both online and offline.

ID#36

Title: Comparative analysis of listing criteria for hepatocellular carcinoma: Milan criteria versus Ontario criteria – A UNOS analysis

Christian Magyar - University Health Network

Introduction

Liver transplantation (LT) is a curative treatment for hepatocellular carcinoma (HCC). In this study, we compare the survival of patients listed within Milan criteria (MC) and the Ontario criteria (OC).

Methods

Patients with HCC with available tumor information were selected from the United Network for Organ Sharing (UNOS) registry. These patients were divided into two groups based on MC (single lesion ≤5cm or 2-3 lesions ≤3cm) and OC (total tumour volume [TTV] ≤145cm3 and AFP≤1000ug/L). Survival analysis of estimates (Kaplan-Meier curve) and effects (Cox proportional hazard models) were performed.

Results

29,086 patients were included: median (IQR) age 60years (55,64), male 22,303 (77%), body-mass index 28.5kg/m2 (25.3,32.3), and Model of End-stage Liver Disease (MELD) 10 (8,14). 27,829 (96%) patients were classified as within MC-within OC (+MC+OC), 391 (1%) within MC-beyond OC (+MC-OC), 771 (3%) beyond MC-within OC (-MC+OC), and 95 (1000ug/L; n=419) was associated with increased mortality (HR 1.60; 95%CI 1.41,1.82), while TTV>145cm3 (n=71) showed no significant association (p-value=0.553). Compared to +MC+OC, the categories +MC-OC (aHR 1.83; 95%CI 1.60, 2.10; p-value 1000 ug/L).

Conclusion

Incorporating AFP appears to improve risk stratification of patients with HCC listed for LT. However, potential statistical biases stemming from sample size could have impacted the TTV analysis.

ID#41

Title: Successful use of maintenance eculizumab during pregnancy in a kidney transplant recipient with history of atypical hemolytic uremic syndrome secondary to complement factor H gene mutation – a case report and review of literature

Somaya Zahran - McGill University

Background

Eculizumab is a humanized monoclonal antibody targeting C5, used in the treatment of atypical hemolytic uremic syndrome (aHUS). It is accepted as maintenance therapy for the prevention of recurrent aHUS post kidney transplant (KTx), however, there is limited clinical experience with its use during pregnancy.

Methods

Pubmed search was conducted for reports of prophylactic use of eculizumab in aHUS pregnant KTx recipients between 1993 and 2024. Thirty-five articles were found, of which only three fulfilled our criteria, including 3 cases in total (summary provided in table 1). We also report an additional case report in our institution with data on 8 years follow-up.

Results

We report case of a 36-year-old woman with a history of end stage renal disease secondary to aHUS in 2009. Complement testing confirmed a mutation in the complement factor H gene. She was treated with hemodialysis, plasmapheresis, rituximab and vincristine. She remained on hemodialysis until she received a standard-criteria deceased donor KTx in 2013. Eculizumab was administered in the perioperative period and thereafter as maintenance therapy. In 2016, she had a planned pregnancy. Eculizumab maintenance was continued during pregnancy and aspirin 80 mg daily was prescribed for pre-eclampsia prevention. Biomarkers of hemolysis and kidney function were closely monitored. Despite the development of acute kidney injury likely secondary to calcineurin toxicity and pre-eclampsia which led to preterm delivery at 33 weeks gestation, the patient delivered a healthy infant and had well-preserved allograft function with no recurrence of aHUS during pregnancy nor in the 8 years postpartum.

Conclusion

The use of eculizumab in a pregnant KTx recipient is rare. Eculizumab is considered safe during pregnancy and during lactation as it is thought to not be transmitted through breastmilk. Maintenance eculizumab is a plausible option for prevention of aHUS recurrence in pregnant women who received KTx.

ID#42

Title: Factors Limiting Referral for Pre-Tranplant Evaluation in a Chronic Kidney Disease Clinic

Sacha De Serres - CHU de Québec

Introduction: With the increased use of marginal organs for marginal recipients, barriers and heterogeneity in referral become a challenge. We aimed to characterize, in a tertiary chronic kidney disease (CKD) clinic, patients considered eligible/referred for pretransplant evaluation versus patients of undetermined/unreferred status.

Methods: Single-center, retrospective cohort study of patients registered to the CKD clinic as of June 2021. Patients aged > 80 years were excluded. We assessed differences between groups using t and chi-squared tests.

Results: 572 patients registered; 395 patients were ≤80 years old. Among them, 203 had a progressive disease, defined as CKD stage V or CKD stage IV with an eGFR projected to reach < 1 5 ml/min/1.73m2 in 5 years. These 203 patients were classified according to the status indicated by the CKD clinic medical team: 46 (23%) were considered eligible and/or already referred for pretransplant evaluation, 78 (38%) were considered unsuitable for transplant, and 79 (39%) had an undetermined status. There was no difference in sex, BMI, ethnicity, and living distance from the transplant center between eligible patients and those with undetermined status. However, patients with undetermined status were older (66±11 vs. 58±13 yrs, p < 0 .01), had a higher eGFR (15±5 ml/min/1,73m2 vs 12±4, p < 0 .01), a higher number of cardiovascular & metabolic comorbidities (2.4±1.6 vs. 1.6±1.3, p < 0 .01), and a higher risk score of 3-year mortality (Dusseux score 5.9±3.7 vs. 3.2±3.0, p < 0 .01). Nonetheless, 43/79 (54%) of these undetermined patients were in the lowest Dusseux risk score group (score ≤6), predicting a 3-year mortality in dialysis of 30%, considered suitable for kidney transplantation evaluation according to a large multicenter, validated study (Kidney Int 2015, 88(1):121-9).

Conclusions: A sizeable proportion of theoretically eligible candidates for pretransplant evaluation had an undetermined status for referral. Age and number of comorbidities were significantly higher in these patients compared to those considered eligible for referral.

ID#43

Title: Liver transplantation outcomes within the practice of medical assistance in dying (MAiD): a retrospective cohort study

Olivia Ganescu - McGill University Health Centre

In 2017, deceased organ donation after medical assistance in dying (MAiD) began in Quebec. MAiD organ recovery mirrors donation after circulatory death (DCD), but donor characteristics and logistics differ. Canadian MAiD donor liver outcomes data remains scarce. This study aimed to compare recipient outcomes of liver transplantation from MAiD-DCD, standard DCD, and donation after brain death (DBD). A single-centered retrospective study, including all adult liver transplant recipients, was performed between January 2018 - March 2024. Kaplan-Meier survival analysis and multivariate Cox regression were used with donor/recipient variables. Overall, n=207 patients (19 MAiD, 15 DCD, 173 DBD) underwent liver transplantation. In contrast to other groups, all MAiD donors suffered from neuromuscular degenerative diseases. The only pre-operative differences were median donor age (59 MAID, 37 DCD, and 54 DBD, p=0.00035), and median donor BMI (20.3 MAID, 22.4 DCD, 25.7 DBD, p=0.00011). There were no major differences in peri-operative characteristics. Graft loss < 9 0 days occurred in n=3 (15.7%) MAiD, n=16 (9.2%) DBD, n=0 DCD (p=0.28). 2 of 3 MAiD recipients that required re-transplantation were found to have graft portal vein thrombosis. The most common complications were biliary strictures: n=9 (47.3%) MAID, n=3 (20%) DCD, n=77 (44.5%) DBD (p=0.590), with most being extra-hepatic. Kaplan-Meier analysis of graft and patient survival showed no statistically significant differences between groups (p=0.65 and p=0.17, respectively). Cox models assessing for graft failure were significant for recipient patient age (HR: 0.94, 95% CI [0.89-0.99],p=0.027) and fascia left open at the initial operation (HR: 19.5, 95% CI [4.8-79.3], p=3.3e-5). Using MAID as the reference group, there were no significant differences in patient mortality. Albeit in a small sample, MAiD liver results appear to be comparable to the standards of care. Further validation through a Canadian collaborative is underway, without current evidence to refute the use or indication of MAiD liver grafts.

ID#44

Title: Implementation of home-based daily spirometry in the early post-lung transplant period

Lisa Wickerson - University Health Network

Background: Daily monitoring of lung function in the early post-lung transplant (LTx) period can improve early detection of graft dysfunction. In-person lab testing is time and resource intensive for patients and providers. The aims of this study were to assess adherence and usability of home spirometry, and explore correlation with in-lab spirometry.

Methods: Handheld spirometers (MIR Spirobank SmartTM) were provided to LTx recipients upon hospital discharge or at their first post-transplant clinic visit. Spirometry data (FEV1, FVC, FEV1/FVC, FEF 25-75) were manually entered after a daily prompt into a custom-designed module located within the electronic medical record (EMR) patient portal (EpicTM). Results were integrated into clinical workflows for clinicians to view. Adherence was measured as the proportion of entered values vs. expected values. Usability of devices and the data entry system was assessed with a daily question during data entry and discussions with patient partners. Analyses were done to assess mean difference (t-test) and correlation coefficient between in-lab and at-home spirometry results.

Results: Data was analyzed for the initial 16 participants (87% male, 56 ± 13 years, 69% interstitial lung disease) in the first 3 months post-transplant. Median (IQR) daily adherence rate was 81 (47-91)%. All participants reported ease of use of the device and system. There was no significant difference between mean FEV1 values between groups (mean difference 0.096L ± 0.22, $p = 0.1$) with strong correlation between home and lab spirometry measurements ($r = 0.96$, $p < 0.0001$).

Conclusion: LTx recipients had a high rate of adherence and reported good usability of a home spirometry device and electronic reporting system. In-lab and home measurements had good correlation. Future directions include direct device-EMR integration and the development of alerts for abnormal or missed values to improve early detection of graft dysfunction and target opportunities to improve adherence.

ID#45

Title: Literacy Level of Renal, Hepatic, and Pulmonary Transplant Patients Before and After Therapeutic Patient Education in Quebec

ASTRID BACLE - CHU Rennes

Background

Health literacy (HL) is crucial for transplant patients, associated with better post-transplant management. Therapeutic patient education (TPE) promotes autonomy, but low HL can hinder this learning. This study examines whether HL levels vary among transplanted organs and assesses the effect of TPE on HL.

Methods

Prospective monocentric study evaluating HL using the STOFHLA score before and after TPE. Demographic data were extracted from medical records.

Results

Among the 98 included patients (mean age: 56.6 years; 40.8% female), distributed among renal transplants: RT (n=38), pulmonary: PT (n=36), and hepatic: HT (n=24), no significant difference in HL was observed before TPE. After TPE, all groups showed a significant increase in HL (RT: 26.6 vs 31.1, p=0.0406; HT: 25.2 vs 31.5, p=0.0157; PT: 25.1 vs 30.9, p=0.0096). Additional analyses revealed lower HL scores among foreign patients, non-university graduates, and those without private insurance.

Discussion - Conclusion

Before TPE, HL levels were similar among groups of transplant patients, highlighting the importance of uniform education. TPE leads to a significant improvement in HL, indicating its effectiveness in enhancing the health skills of transplant patients. However, disparities persist, with lower HL scores among foreign patients, less educated individuals, and those without private insurance. Adapting TPE to meet the needs of these vulnerable populations is necessary.

ID#46

Title: Comparing physical function pre- and post-COVID-19 pandemic onset in solid organ transplant recipients

Jad Fadlallah - University Health Network

Background: The COVID-19 pandemic related restrictions and immunocompromised status of Solid Organ Transplant Recipients (SOTR) may have limited their engagement in physical activities, potentially impairing their physical function (PF). This study evaluates differences in Patient Reported Outcome Measure Information System PF (PROMIS-PF) scores following the pandemic onset compared to pre-pandemic times.

Methods: Cross-sectional convenience sample of prevalent(>30-days post-transplant) adult SOTR(kidney, kidney-pancreas and liver), recruited between 2016-2024. Demographic information was self-reported, clinical data extracted from health records. Participants completed PROMIS-PF as Short-Form-29 or Computer Adaptive Testing using an electronic data capture platform. The primary exposure "assessment era" categorizes participants into pre-pandemic(PRE) and post-pandemic(POST) based on the date they completed the questionnaires relative to March 2020. The second exposure "transplant era" additionally considers the transplant date, dividing the POST group into those transplanted before(POST-1) and after(POST-2) the pandemic onset, resulting in three groups. The outcome was PROMIS-PF (lower scores=worse PF).

Results: Among 707 participants, 442(63%) were male, 256(36%) had diabetes, mean(SD) age was 53(15) years and median(IQR) time since transplantation at enrollment was 5.5[1; 12] years. Mean(SD) PROMIS-PF scores were 48(9) for PRE(n=496) and 45(9) for POST(n=211), $p < 0.001$. Scores were 48(9) in PRE, 47(8) in POST-1(n=123), and 42(9) in POST-2(n=88), $p < 0.001$. Multivariable regression, adjusted for organ type, age, sex, ethnicity, education, socioeconomic status, comorbidities, and time since transplant, showed no significant difference between POST and PRE (reference:PRE, coeff -1.4; 95% CI, -3.0 to 0.2;P=0.09), or between POST-1 and PRE (coeff 1.2; 95% CI, -0.8 to 3.2; P = 0.2). However, POST-2 had significantly lower scores compared to PRE (coeff -4.4; 95% CI, -6.6 to -2.2; $p < 0.001$).

Conclusion: SOTR transplanted post-pandemic onset(POST-2) exhibited lower PF than those transplanted pre-pandemic (PRE and POST-1). This highlights the need for interventions to improve PF recovery in this population.

ID#47

Title: Pain interference and social participation among liver transplant recipients

Maria Pucci - University Health Network

Background: Bodily pain can be linked to poor quality of life (QOL) and limited social participation. Social participation, defined as the ability to perform one's usual social roles and activities, is a patient-valued QOL domain often restricted in liver transplant recipients (LTRs). We aimed to explore the association between pain interference (PI) and social participation (SP) among LTRs.

Methods: We analyzed cross-sectional data from a convenience sample of adult LTRs at Toronto General Hospital. PI and SP were assessed using Patient-Reported Outcome Measurement Information System (PROMIS) computer adaptive testing (CAT). We defined moderate/severe PI as a T-score > 60 and low SP as a T-score < 45. We used Spearman correlation analysis to explore the relationship between SP and PI and employed multivariable linear and logistic regression to further examine the association, after adjusting for covariables (age, sex, marital status, racialized status, comorbidity, albumin, hemoglobin, bilirubin, INR, AST, serum sodium, depression, and fatigue). Multiple imputation was used to address missing data.

Results: The mean (SD) age of the 234 participants was 56 (15) years, 65% were male, and 74% were white. The median (IQR) years since transplant was 4 (10). The mean (SD) SP and PI scores were 50 (9) and 51 (10), respectively. A moderate negative correlation existed between SP and PI (rho= -0.58, p < 0 .001). This association remained significant in multivariable linear regression analysis (ß= -.221, p < 0 .001; 95% CI: -.321 – -.121). Participants with moderate/severe PI were more likely to report low SP compared to those with no or mild PI in multivariable logistic regression analysis (OR= 4.96, p= 0.001; 95% CI: 1.92 – 12.8).

Conclusion: LTRs experiencing significant PI reported more limited SP than those with low PI. Future studies should assess the impacts of pain and pain management on social health following transplantation.

ID#48

Title: Optimization of extended criteria renal transplantation: A clinical practice guideline

Joanna Dionne - McMaster University

Background: Kidney transplant remains the preferred treatment for patients with end stage kidney disease leading to improved life expectancy when compared to remaining on dialysis. However, there is a gap in the number of kidneys available for transplantation. The purpose of this clinical practice guideline (CPG) is to provide recommendation on the utilization of extended criteria donor (ECD) for kidney transplant.

Methods: A steering committee (SC) was formed to address the utilisation of ECD kidneys. Standardized GRADE (grading of recommendations, assessment, development and evaluation) guideline methodology was used.

Results: The following recommendations were made:1) We suggest transplanting kidneys from ECD over remaining on the waitlist and continuing with dialysis (conditional recommendation, very low certainty of evidence); 2A)We suggest utilizing kidneys from non-ECD for transplantation when available (conditional recommendation, very low certainty);2B) We suggest utilizing kidneys from ECD in selected transplant candidates (conditional recommendation, very low certainty);3) We suggest either acute kidney injury (AKI) or non-AKI kidneys can be used based on clinician assessment and donor factors (conditional recommendation, very low certainty);4) We suggest that donor kidneys with AKI from either non-ECD or ECD be used for kidney transplantation (weak recommendation, very low certainty); 5A) We suggest that organs from younger kidney donors be used whenever they are available for kidney transplantation (conditional recommendation, very low certainty); 5B) We suggest that organs from older kidney donors be used in selected transplant candidates who may derive benefit from them (conditional recommendation, very low certainty); 6A) We suggest using neurological determination of death (NDD) kidneys when available for transplantation (conditional recommendation, very low certainty); 6B) We suggest using donation after circulatory death (DCD) kidneys for transplantation, when available, considering candidate characteristics (conditional recommendation, very low certainty).

Conclusion: This CPG provides clinical guidance on using ECD kidneys to improve kidney utilization.

ID#49

Title: AUTOPHAGY INHIBITION AGGRAVATES RENAL MICROVASCULAR INJURY SECONDARY TO ISCHEMIA-REPERFUSION.

Hyunyun Kim - Universite de Montreal

Ischemia-reperfusion injury (IRI) is an integral component of kidney transplantation. Programmed cell death (PCD) of endothelial cells in peritubular capillaries (PTC) post-IRI is a major predictor of long-term loss of renal function. We have shown that caspase-3-deficient mice show reduced PTC apoptosis post-IRI and preserved long-term renal function. Autophagy is known to prevent apoptosis but its precise role on PTC post-IRI remains unclear. Here, we characterize the dynamics of PCD activation and the effect of autophagy inhibition on the renal microvasculature post-IRI.

GFP-LC3 mice were subjected to unilateral renal artery clamping for 30 minutes with contralateral nephrectomy. Mice were injected intraperitoneally with PBS or chloroquine (CHQ) to inhibit autophagy, on surgery day and every day until sacrifice. Mice were euthanized from 1 to 21 days post-surgery. Kidney function was assessed by measuring BUN levels. Apoptosis and necroptosis were measured by immunohistochemistry (IHC) for cleaved caspase-3 and pRIPK3 respectively. Autophagy was evaluated through GFP-LC3 puncta using confocal microscopy. PTC rarefaction, myofibroblast accumulation, and collagen deposition were assessed at 21 days by IHC for MECA-32, α-smooth muscle actin (α-SMA) and Sirius red staining, respectively.

PTC showed sustained apoptosis over a period of 1 to 21 days after renal IRI. Necroptosis exhibited a transient increase at 1-2 days post-injury, returning to baseline levels by day 7. Autophagy was not increased in whole phases of renal IRI (from 1 to 21 days). Yet, blocking autophagy with CHQ increased PTC apoptosis at 21 days, but had no effect on PTC necroptosis. Microvascular rarefaction was increased in the CHQ-injected group. This was associated with increased renal fibrosis, α-SMA, and collagen deposition within the PTC.

These findings highlight the significant role of PTC autophagy in regulating microvascular integrity and emphasize the predominant influence of microvascular injury and rarefaction as drivers of progressive renal damage and fibrosis post-IRI.

ID#50

Title: Effectiveness of Therapeutic Patient Education in Improving Health Literacy among Renal Transplant Patients: A Comparative Study between France and Canada

ASTRID BACLE - CHU Rennes

Background: Health literacy (HL) plays a crucial role in post-transplant patient management, closely associated with improved healthcare outcomes. Therapeutic Patient Education (TPE) is pivotal in promoting autonomy; however, its effectiveness may vary depending on healthcare practices. This study focuses on renal transplant patients and aims to explore differences in HL levels before and after TPE activities between two healthcare facilities located on opposite sides of the Atlantic.

Methods: A prospective study was conducted in two hospitals in France and Canada. HL levels of renal transplant patients were assessed using the S-TOFHLA questionnaire, scored out of 40 points, before and after TPE sessions, two months post-hospital discharge.

Results: A total of 38 French patients and 45 Quebecois patients were included in the study. No significant demographic differences were found between the two patient cohorts. Regarding HL levels, no significant differences were observed, both before (26.6 for France and 28.9 for Canada) and after (31.05 for France and 32.27 for Canada) ($p > 0.05$) TPE sessions. In both facilities, an increase in HL level was noted after TPE, with an increase of 3.378 ± 2.134 points in France ($p = 0.1171$) and 4.447 ± 2.134 points in Canada ($p = 0.0406$).

Conclusion: This study underscores the importance of TPE in enhancing HL levels among renal transplant patients, both in France and Canada. These findings highlight the effectiveness of TPE programs in enhancing healthcare competencies among renal transplant patients, irrespective of geographical context. They also underscore the importance of developing effective TPE practices tailored to the needs of renal transplant patients, regardless of their treatment location.

ID#51

Title: A Retrospective Review of Belatacept Outcomes in Kidney Transplant Recipients

Danielle Blahitka - Saskatchewan Transplant Program

Background: Belatacept is a unique immunosuppressant that selectively targets a co-stimulatory pathway involved in T-cell activation. Potential advantages include minimizing calcineurin inhibitor toxicity, mitigating donor-specific antibodies (DSA), and promoting adherence with a convenient once monthly infusion schedule. Increased utilization of belatacept in our program prompted a need to evaluate its outcomes.

Methods: In April 2024, a retrospective chart review was conducted for patients treated with belatacept since 2020. Data collection included start date, indication, outcomes, and causes for discontinuation. Outcome assessment included trending serum creatinine and DSA changes (for those initiated for this purpose), as well as evaluating adherence where it was a concern. Results were presented descriptively.

Results: Forty patients, either current or past recipients, were assessed. Patients received treatment for a mean of 12.71 months (±3.84), ranging from 1 to 43 months. Primary reasons for initiation were biopsy-proven CNI toxicity (27/40, 67%) and persistent DSA despite triple therapy (18/40, 45%) (Figure 1).

Of the forty patients, thirty-one (77 %) continued belatacept. Reasons for discontinuing included graft failure unrelated to belatacept, T-cell mediated rejection, relocation, access issues, adverse effects, creatinine increase and unrelated death.

Belatacept resulted in the decrease (5/18, 28%) and elimination of DSAs (4/18, 22%) (Figure 2). Serum creatinine remained stable (15/29, 52%) and decreased (11/29, 38%) by a mean of 45 ± 25 umol/L (Figure 3). Of the patients previously experiencing adherence issues, three out of four regularly attend appointments and rarely miss a dose.

Conclusion: Belatacept has proven valuable in preserving graft function by reducing or eliminating DSAs, in addition to serum creatinine stabilization or reduction. It is an alternative immunosuppressive option for those facing adherence issues, exhibiting CNI toxicity and/or as an adjunct for persistent DSAs despite triple therapy. Enhanced access to belatacept in Canada has the potential to significantly benefit renal transplant patients.

ID#52

Title: Eyes Wide Viral: Unveiling Epstein-Barr's Ocular Manifestations in Pediatric Kidney Transplant Recipients

Camille Laroche - Centre Hospitalier Universitrare Sainte-Justine

Forty percent of kidney transplant recipients under 9-years-old are seronegative for Epstein-Barr Virus (EBV) at the time of transplant. EBV poses significant risks to immunosuppressed patients following kidney transplant, as primary infection and uncontrolled latent infection leading to lymphoproliferative disorder (PTLD). Though rare, EBV can also lead to anterior uveitis (AU) and raises challenges in both diagnosis and treatment.

Two cases, both transplanted at 4-years-old developed eye redness and photophobia symptoms compatible with AU alongside high EBV viral load recurrence 2.5-3 years post-transplant. First case was seropositive (D+/R+) and second case was seronegative (D+/R-) at transplant. Both had previous rituximab treatment, the first for adenoids' localized PTLD (Figure 1) and the second one for severe EBV viraemia (Figure 2). The first patient's aqueous humor specimen at ocular presentation was positive for large pleomorphic lymphoid cells, but quantity was insufficient for EBV PCR analysis. Treatment included immunosuppression reduction, topical corticosteroid, brimonidine and cyclopentolate chlorhydrate, oral acetazolamide and obinutuzumab infusion. They had full recovery without visual sequelae 9 months after initial presentation. The second patient had evidence of bilateral uveitis with mixed anterior chamber hypopyon and hyphaemia, keratic precipitate, and vitritis. Anterior chamber fluid sample was EBV PCR positive. They were treated with bilateral orbital floor injections of triamcinolone and topical dexamethasone for 6 months, but persistent EBV viremia and chronic uveitis findings warranted intensification of treatment with rituximab, resulting in decreased plasmatic viral load and improvement of ocular inflammation.

These cases highlight post-transplant EBV viraemia's complexities, particularly in ocular manifestations, where EBV's role might be underestimated. Detecting EBV in ocular tissue is challenging and its presence can mimic other causes of uveitis. EBV AU management in post-transplant recipients remains unclear due to limited literature, emphasizing the need for vigilant monitoring and early intervention to mitigate long-term vision effects.

ID#53

Title: A combined assessment living donor evaluation clinic reduces the evaluation time for potential living donors

Kenan Hallon - Fellow

Background: Living donor (LD) transplant requires comprehensive workup of prospective donors and a protracted evaluation can result. This risks missed opportunities for preemptive transplants, heightened anxiety patients, and donor withdrawal. A streamlined workup process with a combined Urology/Nephrology assessment clinic was created in July 2021 to improve efficiency. The purpose of this study is to examine the impact of the combined LD assessment clinic on the efficiency of donor workup.

Methods: Single-center retrospective study involving all LD's between Jan 2019 and 2023 at the University of Alberta Hospital. Primary outcome: length of LD workup. Two eras of evaluation were defined: Era1 (Jan 2019 - July 2021) and Era2 (Oct 2021 - 2023). July 2021 to Sep 2021 was a washout period when the clinic started and was excluded. Time to approval was compared using a two sided t-test (alpha 0.05).

Results: From 2019 to 2023, 134 donors were approved for donation. Era1 had 63 donors successfully approved for donation with 61 in Era2; 10 donors were approved in the washout era. Compared to Era1, Era2 had a significantly shorter evaluation time (126 vs 275 days, $p < 0.01$). Time from donation approval to transplant was also significantly reduced in Era2 (90 vs 224 day, $p < 0.01$).

Conclusion: LD combined clinic leads to a significantly reduced duration of evaluation, and time to donation. Limitations include single program data with unknown reproducibility. Furthermore, the retrospective nature of this study limits the ability to assess any impact on donor and recipient satisfaction with this donor work up process.

ID#54

Title: Polyomavirus associated trichodysplasia spinulosa in a pediatric kidney transplant recipient

Nivedita Pande - Montreal Children's Hospital

Background: Kidney transplantation entails the use of immunosuppression (IS) to prevent and treat rejection. However, the use of immunosuppressive drugs can predispose the recipients to atypical infections, involving the allograft or other organs such as the skin. Here, we report a case with one such distinct cutaneous infection caused by trichodysplasia spinulosa polyoma virus (TSPyV). Methods : A ten-year-old girl with congenital nephrotic syndrome, reached end-stage renal disease at the age of 8 years and underwent a deceased donor kidney transplant. She received thymoglobulin and methylprednisolone in the peri-transplant period followed by tacrolimus, mycophenolate mofetil (MMF), and prednisone as maintenance IS. Results: At 14 months post-transplant, she was noticed to have diffuse, spiculated white follicular papules on the face progressively involving the arms, trunk, and thighs. A provisional diagnosis of keratosis pilaris was made. She was started on topical tacrolimus cream and a moisturizer. A skin biopsy on the posterior aspect of the right arm was done as the cutaneous lesions became extensive and did not respond to the topical therapy. Histology showed dilated hair follicles and inner root sheath-like keratinocytes which were eosinophilic with purple trichohyalin granules. Paraffin scrolls of the specimen were positive for trichodysplasia spinulosa polyomavirus small T antigen viral gene. Thereafter, the dose of MMF was decreased from 800 mg per m2 per day to 530 mg per m2 per day. The lesions did not improve and oral valganciclovir was started at a dose of 15 mg per kg per dose twice a day. MMF was replaced with leflunomide; the dose for 20-40 kg weight band is 10 mg once a day. Conclusion :Trichodysplasia spinulosa is a rare and distinct polyoma virus infection affecting the skin of recipients of solid organ transplant. Definitive diagnosis is by histology. The disease is slow in progression, difficult to treat, and can be extensive.

ID#55

Title: Urinary IL-6 : One Step Closer to Resistant Rejection Identification

Camille Laroche - Centre Hospitalier Universitrare Sainte-Justine

Background Acute T cell-mediated rejection (TCMR) is a key contributor of graft failure, especially when it is resistant to first-line treatment, as sustained inflammation during initial treatment phase leads to chronic rejection and declining kidney function. Transition from acute to chronic allograft inflammation involves superimposing lymphocytes T helper 17 (Th17), with IL-6 influencing the shift from acute to chronic changes and dedifferentiation of pro-tolerant Treg to pro-inflammatory Th17 cells. We hypothesized that steroid treatment resistance could be explained by more established Th17 presence, translating in higher urinary IL-6 level. Methods Urine samples were prospectively collected from pediatric kidney transplant recipients on days of surveillance and indication biopsy and stored in local biobank. Urinary IL-6 was measured using ELLA multiplex assay. Early and late rejection were respectively defined as diagnosed ≤ 1 year and > 1 year post transplant. Results Urinary IL-6/Creatinine (uIL-6/Cr) ratio was measured in 65 samples from patients with normal (n=20), IFTA (n=15) and rejection (n=30) diagnosis. Rejection group included borderline TCMR (n=24) and TCMR graded ≥ Banff 1A (n=6) (Table 1). A trend was observed with median uIL-6/Cr being higher in the rejection group (n=30) and borderline subgroup (n=28) compared to normal (n=20) group (p=0.07). Median uIL-6/Cr was higher in TCMR ≥ Banff 1A (n=6) compared to normal group (0.37 versus 1.30, p = 0.01). Median uIL-6/Cr was higher in late TCMR (n=13, including borderline) compared to early TCMR (n=17, including borderline) with greater difference observed between normal and late TCMR groups (p = 0.05) (Table 2). Conclusion Our results suggest that uIL-6/Cr could be used as a non-invasive biomarker for TCMR Banff 1A and greater. uIL-6/Cr could be used as a prognosis tool for predicting treatment responsiveness, as late TCMR generally presents with a more established rejection process and resistance to first line treatment.

ID#56

Title: Comparative analysis of tacrolimus kinetics in identifying acute cellular rejection after heart transplantation

Chengliang Yang - St Paul's Hospital

Background Graft rejection following cardiac transplantation remains a significant source of morbidity and mortality. Acute cellular rejection (ACR), the most prevalent form, typically occurs within the first six months post-surgery. Tacrolimus, an immunosuppressant, is often administered with other agents to prevent acute cardiac allograft rejection. This study aimed to assess blood tacrolimus concentration in patients with and without ACR.

Methods Blood samples were collected during routine monitoring after adult heart transplantations at St. Paul's Hospital in Vancouver. Participants were enrolled in the Multi-Marker Blood Test for Acute Cardiac Transplant Rejection (HEARTBiT, NCT03575910), a prospective observational study conducted between 2018 and 2020. Tacrolimus blood concentrations were measured using tandem mass spectrometry. Rejection severity was determined through histopathology grading of endomyocardial biopsy (EMB) samples according to ISHLT guidelines, excluding isolated antibody-mediated rejection. Blood samples were matched with EMB collection times within a range of ±1 day.

Results A total of 315 EMBs were analyzed from 41 consecutive heart transplant recipients (28 male and 13 female, median age = 60, IQR = 14 years) over thirteen scheduled follow-up visits within the first 180 days post-transplant. Overall, 13 episodes of ACR were identified: 9 within 90 days and 4 between 91 and 180 days post-transplantation. In the first 90 days post-transplant, tacrolimus concentrations were significantly lower in the 2R group than in the 0R ($p = 0.0069$) and 1R ($p = 0.0292$) groups. No significant difference was observed between groups from 91 to 180 days post-transplant.

Conclusion Monitoring tacrolimus levels early in the post-heart transplant period may help identify patients at risk for ACR. However, tacrolimus concentration monitoring may not effectively detect ACR between 4 to 6 months post-transplant. Our results are preliminary, and further studies with larger sample sizes are needed to better understand the factors contributing to early post-transplant rejection.

ID#57

Title: Calculated Probability of Recipient Compatibility (cPRC): A novel index to determine HLA compatibility for organ allocation

Jenny Tran - University of British Columbia

Background: Currently there is no metric that assesses a transplant candidate's HLA compatibility within a donor pool. Here, we introduced calculated Probability for Recipient Compatibility (cPRC), a novel index which estimates the likelihood of finding a well-matched (low mismatch) donor. We applied cPRC to evaluate the potential impact of HLA matching on ethnic disparity using the more flexible strategy of eplet versus conventional antigen-based compatibility assessment.

Methods: For each candidate on the kidney waitlist (n=457), HLA matching was performed against all deceased donors (n=138) identified during a 1-year timeframe in BC. Eplet mismatch (EpMM) was determined using the single-molecule approach, and low EpMM was DR < 7 and DQ < 9 . Low antigen mismatch (AgMM) was 0 DR and 0 DQ mismatches. cPRC was determined for each patient and calculated as the number donors that were low-mismatch divided by all donors. Patients considered "hard-to-match" were those that never had a low-mismatch donor (cPRC=0%).

Results: Overall, more candidates could find a well-matched donor when evaluated using eplet (91%) versus antigen-based (78%) matching. The median cPRC was greater when assigned using eplet (6.5%) compared with antigen (1.4%) (Fig1), indicating that a higher number of donors were well-matched for each candidate when assigned using the eplet approach. Furthermore, more patients were considered hard-to-match for AgMM (22%) than EpMM (9%). Ethnicities of patients were 46% Asian, 40% White, and 14% Other in this study cohort. Non-white ethnicities were more likely to be considered hard-to-match when evaluated using AgMM but the impact of this disparity was attenuated when considering EpMM (Fig2).

Conclusion: cPRC represents a standardized index that could be applied to different HLA matching strategies to estimate the probability of finding a well-matched donor in a given population. LA compatibility appears to be ethnically determined, but EpMM decreases the proportion of candidates considered hard-to-match compared to AgMM.

ID#58

Title: Impact de l'administration de desmopressine sur la survenue de complications post-biopsie rénale chez les patients avec un greffon rénal à l'Hôpital Maisonneuve-Rosemont

Jean-Marc Lalande - Université de Montréal

Objectif : La biopsie rénale comporte un avantage diagnostique, bien qu'elle soit une procédure invasive comportant un risque non-négligeable de saignement. Afin de réduire ce risque, la desmopressine (DDAVP) peut être utilisée chez les patients à plus haut risque comme les insuffisants rénaux. Or, il demeure inconnu si l'utilisation du DDAVP est associée à une diminution du risque de saignement chez les greffés rénaux.

Méthodes : Une étude de cohorte rétrospective a été menée sur 185 patients adultes ayant eu une biopsie de greffon rénal à l'hôpital Maisonneuve-Rosemont entre 2016 et 2021. L'utilisation de la DDAVP et la survenue péri-biopsie de complications hémorragiques et hémodynamiques, tout comme leur investigation (p. ex : radiologique) et traitement, ont été étudiées. Les caractéristiques des patients ayant reçu la DDAVP ont été comparés à ceux ne l'ayant pas reçu.

Résultats : Les caractéristiques de base de la cohorte étaient les suivantes : âge moyen 52,5±12,9 ans; 37,3% de femmes; 71,9% avec IRC de stade 3 ou plus. Un total de 56 patients (30,8%) a reçu la DDAVP. En pré-biopsie, les patients du groupe DDAVP avaient une anémie plus sévère (Hb moyenne 100,7±18,5 vs 123±16,1 g/l) et une dysfonction rénale plus importante (DFGe 27,9±20,4 vs 52,5±19,8 ml/min/1.73m2). En post-biopsie, les patients du groupe DDAVP ont eu un besoin transfusionnel plus important (4 vs 0 transfusions) et une survenue plus grande d'hyponatrémie (10 vs 4 épisodes). La proportion de patients avec une chute d'Hb supérieure à 10 g/L était similaire entre les 2 groupes (8,5% vs 10,4% pour le groupe DDAVP).

Conclusions : L'utilisation du DDAVP chez les greffés rénaux semble plus fréquente chez ceux à plus haut risque de saignement. Les complications hémorragiques sont rares dans cette population. La survenue d'une hyponatrémie post utilisation du DDAVP doit être prise en considération comme complication potentielle.

ID#59

Title: Characterizing renal tubular epithelial injury during donation after cardiocirculatory death and possible amelioration with PKX-001

Yara Azizieh - Dalhousie University

Background: Kidney transplantation is the treatment for end-stage renal disease, with donors after cardiocirculatory death (DCD) addressing the organ shortage. DCD kidneys face ischemia-reperfusion injury, leading to delayed graft function (DGF). Organ machine preservation (MP) has shown promise in reducing DGF compared to static cold storage (SCS). PKX-001, a synthetic antifreeze protein, exhibits a potent anti-inflammatory and antioxidant effect. This study aims to characterize the renal epithelial damage in DCD kidneys and evaluate the efficacy of MP in preserving tubular integrity compared to SCS. Additionally, we explore the potential benefits of incorporating PKX-001 during flushing.

Methods: A DCD rat model was established, with kidneys allocated to receive PKX-001 (5mg/mL) or saline during in-situ flush. Organs underwent hypothermic preservation (~4°C) in either SCS or hypothermic machine perfusion (HMP) for 24h, forming four groups (n=6): Group 1: SCS + saline, Group 2: SCS + PKX-001, Group 3: MP + saline, and Group 4: MP + PKX-001. Perfusate samples were quantified for N-acetyl-b-D-glycosaminidase (NAG). Tissue samples will be stained for Kidney Injury Molecule-1 and cleaved caspase-3 to assess tubular damage. Cytokines, chemokines, and cleaved caspase-3 will be quantified in tissue lysate. In a second experiment, kidneys from groups 1 and 4 underwent normothermic machine preservation (~37°C) for 2 hours, simulating reperfusion.

Results: The rat DCD model and kidney preservation system were established. Preliminary findings reveal increased NAG activity over 24 hours, peaking after reperfusion ($P \leq 0.0001$), with attenuation in kidneys preserved on MP and treated with PKX-001 ($P \leq 0.001$). Cleaved caspase-3 activity during cold preservation was consistent across groups but reduced after reperfusion in kidneys preserved on MP with PKX-001 (not significant). Blinded pathologist grading of tissues reveal a lower degree of acute tubular necrosis on PKX-001 preserved groups. Futher histology analysis will provide more insights into tubular tissue damage and the potential protective role of PKX-001.

ID#60

Title: Longitudinal analysis of immediate post-transplant symptom frequency in kidney and liver transplant recipients

Ana Samudio - Multiorgan Transplant Program and Division of Nephrology

Background: We compare frequency of physical and psychological symptoms among incident kidney (KT) and liver transplant (LT) recipients using Patient Reported Outcomes Measurement Information System (PROMIS) computer adaptive tests (CAT).

Methods: Longitudinal convenience sample of incident (60 or <= 40 indicate moderate-severe symptom severity or function impairment, respectively.

Results: Of 216 participants, 133(62%) were KT, 133(62%) were male, and mean(SD) age was 52(14) years. Median (interquartile range) time after transplant at enrolment was 6(4,10) days. At baseline, all domain T-scores were significantly higher for LT vs KT recipients. At week 12, this difference disappeared for pain interference, anxiety, and depression. At week 24, T-scores neared the U.S. general population mean and differences were non-significant except for sleep disturbance (Table 1). At baseline, the proportion of patients scoring at moderate-severe symptom severity or function impairment was significantly higher for LT than KT recipients for all domains. At week 24, only sleep disturbance and physical function remained significant (Table 2).

Conclusion: LT recipients have greater symptom burden immediately post-transplant than KT recipients. By week 12, differences disappear for pain interference, anxiety, and depression. By week 24, only sleep disturbance and physical function impairment remained significant. Systematic symptom assessment and support may help post-transplant recovery.

ID#61

Title: Assessing social difficulties among liver transplant recipients using the “Social Difficulties Inventory”

Aghna Wasim - University Health Network

Background: Liver transplant (LT) recipients experience challenges in their social life (e.g., social relationships; recreational activities; financial concerns; self-care). Such difficulties can be assessed using the Social Difficulties Inventory (SDI), originally developed among patients with cancer. We evaluate the reliability and validity of SDI and its subscales in LT recipients.

Methods: A cross-sectional, single-centre convenience sample of adult LT recipients completed SDI and legacy questionnaires (SF-36 social functioning; role limitations due to physical and emotional problems; physical functioning domains; EQ5D5L usual activities). Sociodemographic data was self-reported. Clinical data was obtained from medical records. For SDI items, participants are asked to rate difficulty experienced as “no”, “a little”, “quite a bit” or “very much”. 16 items yield SD-16 and its subscales: Everyday Living (EL), Money Matters (MM), and Self and Others (SO). Cronbach’s alpha was used to assess reliability. Spearman correlation between SD-16, its subscales versus “legacy” scores was used to evaluate convergent validity. Known group comparisons between groups expected to yield different SD-16 scores (based on literature or clinical experience) were also performed to support construct validity.

Results: 117 LT recipients (mean(SD) age 55(15) years), 32% female, completed SDI. EL, MM, SO subscales and SD-16 showed good internal consistency (α = 0.90, 0.78, 0.82, 0.90, respectively). SD-16 and EL scores were strongly correlated with SF-36 social functioning (r= -0.75, -0.73) and EQ5D5L usual activities (r=0.68, 0.79). MM and SO scores were moderately correlated with SF-36 social functioning (r= -0.43, -0.55). SD-16 scores were significantly different among groups with low vs high fatigue, financial stability, and depression, confirming most hypotheses.

Conclusion: These results suggest that SD-16 and its subscales have good reliability and construct validity among LT recipients. SD-16 could be used in clinical care to identify LT recipients who may be at risk of social difficulties and may benefit from further assessment.

ID#62

Title: Lung preservation at 10oC protects cellular membranes, increases antioxidant capacity, and promotes metabolic activity in a cell culture model

Tanroop Aujla - University Health Network

Background: Recent pre-clinical and clinical studies have demonstrated that cold static storage at 10oC may represent the new standard for donor lung management and help improve patient outcomes. However, the protective cellular mechanism(s) conferred by 10oC preservation compared to traditional 4oC preservation are still unclear. Characterizing these protective pathways may aid in developing novel strategies for donor lung preservation. Methods: Human pulmonary microvascular endothelial cells (HPMECs) and bronchial epithelial cells (BEAS2B) were cultured to sub-confluence and then incubated in Perfadex® solution at 4oC or 10oC for 4h, 24h, or 48h to simulate varying degrees of cold ischemia. In a subset of experiments, at the end of cold incubation, cells were re-introduced into serum-containing culture medium at 37oC for 4h to simulate warm reperfusion. Results: Storing cells at 10oC significantly reduced LDH release in both cell lines after 48h with and without 4h of warm reperfusion ($P < 0.01$). Total lipid peroxidation and lipid peroxidation normalized to cellular protein content were significantly attenuated in BEAS2B cells stored at 10oC after 48h compared to 4oC ($P=0.02$, $P < 0.001$, respectively). Preservation of BEAS2B cells at 10oC also significantly increased cellular reduced glutathione concentration compared to preservation at 4oC after 48h ($P < 0.05$). In HPMECs, metabolic activity measured using AlamarBlue was significantly increased in cells stored at 10oC after 48h and 4h warm reperfusion ($P < 0.001$). Total ATP concentration in BEAS2B cells remained steady in both 4oC and 10oC groups after 4h and 24h but then significantly declined at 48h in 4oC cells ($P < 0.001$). Conclusion: Compared to the traditional 4oC preservation, these results suggest that 10oC preservation may offer superior cellular membrane protection, antioxidant capacity, and metabolic activity. This data may provide novel insights to improve lung preservation at 10oC by introducing specific cytoprotective agents that support these pathways into the preservation solution.

ID#63

Title: Effect of conversion from tacrolimus to cyclosporine on BK viremia among kidney transplant recipients – the TACCsA-SWITCH study

Hon Shen Png - St Joseph's Healthcare Hamilton

Background: There is no established treatment strategy for BK-polyomavirus (BKPyV) infection among kidney transplant recipients (KTRs) after initial reduction of immunosuppression. In vitro studies suggest an inhibitory role of cyclosporine on replication of BKPyV. We investigated effect of conversion of tacrolimus to cyclosporine (TAC-CsA switch) on BKPyV viral load (VL) among KTRs.

Methods: We conducted a retrospective cohort study with a pre-post study design investigating effect of TAC-CsA switch among KTRs with persistent BKPyV-VL of more than 10,000 IU/ml (equivalent to 4 log10IU/ml) for more than 3 months before TAC-CsA switch. We ensured 6 months of follow up after conversion, between 2020 to 2023. We calculated the slope of change for log-BKPyV-VL in log10IU/ml/month using least-square method and compared the mean results before and after TAC-CsA switch.

Results: 32 patients were included in the analysis. 25 (78.1%) patients had deceased kidney transplantation (KT), and 17 (53.1%) patients received anti-thymocyte globulin. Before TAC-CsA switch, 17 (53.1%) had a change of mycophenolate to leflunomide, 4 (12.5%) and 14 (43.8%) were given cidofovir and intravenous immunoglobulin, respectively. Median time from last immunosuppression adjustment/ therapy given prior to TAC-CsA switch was 112.5 (interquartile range (IQR) 225.75) days. At time of TAC-CsA switch, median BKPyV-VL was 321x10^3 (IQR 2.49x10^6) IU/ml, equivalent to median log-BKPyV-VL of 5.50 (IQR 1.39) log10IU/ml. The mean slope of change for log-BKPyV-VL before and after TAC-CsA switch were 0.304 (95% confidence interval (CI) 0.139, 0.469) and -0.279 (95% CI -0.353, -0.204) log10IU/ml/month respectively. Mean difference between the slopes before and after TAC-CsA switch was -0.583 (95% CI -0.807, -0.358) log10IU/ml/month ($p < 0.001$). 21 (65.6%) patients achieved log-BKPyV-VL improvement of at least 0.2 log10IU/ml/month (equivalent to 16 fold VL reduction in 6-month period) after TAC-CsA switch.

Conclusion: TAC-CsA switch is a useful strategy for difficult-to-treat BKPyV viremia among KTRs.

ID#64

Title: Novel double balloon cannulation for multi-organ procurement

Yigang Luo - University of Saskatchewan

Background: A reliable, fast cannulation of aorta in organ procurement, is critical, especially for DCD (donation after circulatory death). By shortening warm ischemia time, a better donor organ quality is expected against delay graft function (DGF up to 60%) and primary non-function (PNF, up to 5%) in post transplant recipients of DCD organs. Present study used an in vitro simulate set-up to test the concept of a novel reliable and fast cold flushing cannulation for multi-organ procurement. Method: an ArgyleTM Penrose Tubing was used to simulate the abdominal aorta with 4 side holes simulating as celiac artery, superior mesentery artery and bilateral renal arteries, while a PHYCON (I.D. 7.0mm, O.D. 10.7/12.5mm ORAL) endotracheal tube was used as a double balloon cannula in study group, and a traditional MAQUET 21 Fr cannula was used in control group. In the study group, we inserted the double balloon cannula into the simulate abdominal aorta, inflated both balloons, began flushing for 3 minutes. In the control group, a traditional cannula was inserted into the simulate abdominal aorta, a clamp was placed superiorly above the all side holes, and a hand tie was placed distal to the side holes to hold the cannula in place, Similarly flushing was carried out for 3 minutes. The 3 minutes flow volumes in boths group were recorded. In both groups the tests were performed for 10 times. Results: the mean time to the start of flushing was 49.6 seconds in the study group and 61.3 seconds in the control group(P=0.007). There was insignificant differences in flow rates between the control group vs study group (620.5ml vs 575ml), P =4.1). Conclusion: This study proved that a double-balloon cannula might in fact reliably lessen the warm ischemia time, especially when taking into account of time saved in exposing and clamping the upper abdominal aorta.

ID#65

Title: Defining cellular infiltrates in antibody mediated rejection using unbiased proteomics

Maya Allen - University Health Network

Background: Kidney transplantation is the optimal treatment for patients with end-stage kidney disease. Unfortunately, many kidney allografts fail prematurely due to antibody-mediated rejection (AMR). AMR is caused by donor-specific antibodies (DSAs) against human leukocyte antigens (HLA) on the graft endothelium. DSAs may cause injury through endothelial activation, complement activation, or interactions with Fcγ receptors (FcγRs) on immune cells. Intriguingly, 30-60% of DSA-positive kidney allograft recipients never develop rejection, and 30-50% of patients that exhibit AMR do not have any detectable DSAs, suggesting the presence of unidentified contributors to the pathogenicity of AMR. Our goal is to define the molecular mechanisms of AMR and uncover these underlying contributors to injury.

Methods: Indication biopsies from 115 patients with DSA+ AMR, DSA- AMR, no rejection despite having DSAs (DSA+ NR), and T cell mediated rejection (TCMR) were subjected to unbiased proteomics analysis using LC-MS/MS on Q-Exactive mass spectrometer. Significance between groups was established using ANOVA, with $p < 0.05$ considered significant.

Results: We analyzed the glomerular and tubulointerstitial compartments of each biopsy separately. Of the 1203 proteins quantified in the tubulointerstitium, 30 were significantly differentially expressed, and of the 628 quantified in the glomeruli 15 were significantly differentially expressed (ANOVA, $p < 0.05$). Importantly, the expression of complement factors was increased in DSA- AMR tubulointerstitium when compared to DSA+ AMR and DSA+ NR. However, in the glomeruli complement proteins were dominant in DSA+ AMR. Furthermore, proteins downstream of FcγR activation and phagocytosis were increased in the glomeruli of DSA- AMR and DSA+ AMR biopsies when compared to DSA+ NR. In the tubulointerstitium, proteins implicated in phagocytosis were highest in DSA- AMR.

Conclusions: The differential expression of complement proteins and proteins implicated in FcγR-mediated phagocytosis suggests distinct patterns of injury in the two kidney compartments and an unanticipated role of complement and phagocytosis in DSA- AMR.

ID#66

Title: Investigating hepatocyte nuclear factor four alpha as a central regulator of kidney graft repair

Slaghaniya Neupane - University of Toronto

Background

Kidney transplantation is the optimal treatment for end-stage kidney disease. However, ischemia-reperfusion injury (IRI) harms all transplanted kidneys, limiting their short- and long-term survival. Previously, we determined that superior kidney function/structure after IRI is associated with preserved expression of mitochondrial proteins during normothermic ex vivo kidney perfusion (NEVKP). We identified a potential transcriptional regulator of these mitochondrial proteins, hepatocyte nuclear factor 4a (HNF4A), which may present a novel target for kidney repair. Our goal is to determine whether a novel HNF4A agonist, N-trans caffeoyltyramine (NCT), protects kidneys from IRI. We will evaluate the effectiveness of NCT treatment in vitro studying male and female primary proximal tubular cells (PTECs), and in vivo studying male and female mice.

Methods

First, we inhibited HNF4A in primary male and female PTECs, using a pharmacologic or genetic approach. We then assessed gene expression, cell death and mitochondrial function. Next, we treated PTECs with NCT/vehicle and examined cell death and expression of HNF4A target genes. Lastly, male and female mice were subjected to bilateral IRI, and kidney function and structure were assessed on post-operative day 2 and 14.

Results

HNF4A inhibition in vitro increased PTEC death and decreased mitochondrial function (fig.1), while NCT increased the expression of HNF4A and mitochondrial genes (fig.2), suggesting that NCT may be protective. We developed a sex-specific model of bilateral IRI and demonstrated that warm ischemia (27-minutes in males, 40-minutes in females) impairs kidney function on post-operative day 2, indicated by elevated serum creatinine and tubular injury (fig.3A). Mice also developed tubulointerstitial fibrosis on post-operative day 14 (fig.3B).

Conclusions

Based on the preliminary results, HNF4A is important for the metabolic function and viability of PTECs. We will next administer NCT to mice prior to IRI and examine whether HNF4A agonist preserves mitochondria and improves kidney function and structure.

ID#67

Title: Risk Factors for Acute Cellular Rejection Following Orthotopic Liver Transplantation

Monica Dahiya - University of British Columbia

Background: Despite being on immunosuppressive therapies, acute cellular rejection (ACR) is a common occurrence in liver transplant recipients. Several risk factors for ACR have been identified, however the positive predictive power of risk factors varied. In our retrospective, single-center, study, we aim to identify risk factors for ACR in liver transplant recipients.

Methods: Retrospective data was collected from 424 liver transplant recipients that were transplanted at a primary transplant centre in Western Canada. Patients who underwent a liver transplant between Jan 2018 to Dec 2022, were included in the study. Demographic data, biochemical data, and outcomes data (presence of rejection) was obtained via paper transplant charts and electronic medical records.

Results: In the 100 patients included in the preliminary analysis, the median age of transplantation was 58 years, where recipients had a median MELD score at time of transplantation of 16, MELD-Na score of 18, and Child-Pugh score of 9. The etiology of end-stage liver disease (ESLD) was HCC in 19 patients, alcohol in 13 patients, primary sclerosing cholangitis in 13 patients, metabolic-associated liver disease in 11 patients, autoimmune hepatitis in 8 patients, and other/not specified in 17 patients. CMV mismatch was present in 19 patients. ACR occurred in 27 patients. Presence of CMV mismatch was strongly associated with ACR with an odds ratio of 6.15 ($p = 0.001$; 95% CI 2.1 to 19.7). Immune-mediated etiologies of ESLD was positively associated with ACR with an odds ratio of 1.44 ($p = 0.05$; 95% CI 0.47 to 4.3).

Conclusion: Immune mediated etiology of liver disease and CMV mismatch status may predict risk of ACR in liver transplant recipients. In these patients, closer monitoring and earlier consideration of ACR as a cause of liver enzyme abnormalities may provide benefit in earlier diagnosis and treatment of ACR.

ID#69

Title: HSV1: a rare cause of GI tract infection in a patient with kidney transplant

Laura Kim - BC Children's Hospital

A 14-year-old female patient with a history of kidney transplant presented with acute epigastric pain, vomiting, fever, erythema nodosum, acute kidney injury, and elevated lipase at 12 years post-transplant. ESKD was due to bilateral cystic dysplasia. She was receiving standard immunosuppression, had no recent rejection episodes, and had stable kidney function (eGFR 55 mL/min/1.73m2). Abdominal imaging was non-contributory. There were no metabolic or autoimmune risk factors for pancreatitis. She received IV hydration and broad-spectrum antibiotics. Two days later, she developed profuse diarrhea, up to 4 L per day, which persisted despite full bowel rest and antibiotic discontinuation. Investigations revealed down-trending lipase, negative blood, urine, stool, and throat bacterial cultures, negative serum PCR for adenovirus, CMV, EBV, and BKV, and negative infectious diarrhea nucleic acid test panel. Upper and lower endoscopy revealed white patches in the distal esophagus. Biopsy showed patchy active inflammation, sloughed keratinocytes with viral cytopathic effect, and positive HSV1 staining consistent with herpes esophagitis. Rectosigmoidoscopy was normal with no pathologic evidence of HSV. Serum HSV1 and HSV2 PCR were negative. She was HSV immune (serotype unknown) on remote testing. Diarrhea and systemic symptoms improved without antivirals. She received five days of oral valacyclovir due to the severity of presentation once biopsy results were reported. This case highlights an atypical systemic presentation of HSV. HSV is a rare cause of pancreatitis and gastrointestinal tract (GIT) infection in immunosuppressed patients, with the esophagus most commonly affected. We suspect HSV was the cause of pancreatitis and secretory diarrhea: upper GIT presence of HSV was confirmed, but pancreas, small intestine, and upper colon were not biopsied. We hypothesize that GIT HSV involvement may occur without viremia and have a patchy distribution, similar to other herpes viruses like CMV.

ID#70

Title: Association between the histological findings on the pre-implantation biopsies and the renal graft function 1 year post transplantation

Andreea Stepanov - CHUM

Background: Renal biopsies after a transplant allow the physicians to explain clinical deterioration. However, some studies suggest that the initial state of the graft might also have an impact on the renal function. The goal of this study was to determine the association between the histological pre-implantation biopsy findings and the function of the renal graft 1 year post-implantation.

Methods: A retrospective cohort study of 236 patients transplanted between the 30th of June 2008 and 2021 at the University of Montreal Hospital Center was carried-out. A multivariable linear regression model was built with the estimated glomerular filtration rate (eGFR) 1 year post transplantation as the dependent variable and the interstitial fibrosis (evaluated by the VIS imagery system or by the ci score), the ah and ct biopsy scores, the donor age, sex, height, eGFR, hypertension, death cause and smoking status as independent variables.

Results: Severe arteriolar hyalinosis (-19.3 ml/min/1.73 m2 for ah3 vs ah 0-1, 95% confidence interval (CI): -38.4, -0.1), moderate to severe interstitial fibrosis (-18.1 ml/min/1.73 m2 for ci2-3 vs ci 0, CI95% : -34.1, -2.1) and the donor's height (+4.2 ml/min/1.73m2 for every 10 cm, CI95% : 0.6, 7.8) were associated with the eGRF at 1 year post transplantation. The interstitial fibrosis evaluated by VIS did not show a significant association (p=0,219) with the eGFR. Our model explains 16% of the eGFR variability (R2) 1 year after transplantation.

Conclusion: The ci and ah Banff scores evaluated by the pathologist on the pre-implantation biopsy are associated with the graft function 1 year post transplantation after adjustment for the donor variables.

ID#71

Title: Modeling an algorithm for managing interactions with calcineurin inhibitors in solid organ transplantation

Mélodie Richard-Laferrière - Centre hospitalier de l'Université de Montréal

Calcineurin inhibitors (CNIs) are widely prescribed in solid organ transplantation (SOT). Due to their narrow therapeutic index and metabolic pathways, managing drug-drug interactions (DDIs) is challenging in clinical practice. Current therapeutic advisors propose recommendations that can be imprecise, inconsistent and challenging to implement. This study aims to develop clear, consensus-based, and clinically pertinent recommendations for handling DDIs involving CNIs in SOT.

A literature review was conducted to identify drug-drug interactions involving CNIs. A panel of SOT experts comprising 11 pharmacists and one nephrologist was assembled. Employing the Delphi method, these experts were asked to provide guidance for various DDI scenarios involving CNIs. A consensus threshold was set at 70% agreement among the panelists. The first round of discussion, based on the findings of the literature review, was conducted online, with subsequent rounds completed in a roundtable discussion format.

The review of 578 articles revealed 172 molecules or molecule classes that could potentially interact with CNIs. This data formed the basis for 706-statement Delphi questionnaire. Depending on the scenario, one to four rounds were necessary to achieve consensus. Twenty-four distinct management strategies for introducing a weak, moderate or strong CYP 3A4 inhibitor or inducer emerged. These DDI management recommendations take into consideration the potency of CYP 3A4 inhibition or induction, the existing CNIs blood level and the minimal required follow-up. Algorithms for DDIs management with CNIs were developed following the Delphi rounds.

These algorithms have the potential to facilitate the prescription validation process for pharmacists in hospital settings and support clinicians by providing direct applicability to clinical practice.

ID#72

Title: Ethical issues related to the use of less-than-ideal kidneys from deceased donors to improve access to pre-emptive renal transplantation for elderly patients

Marie-Chantal Fortin - Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM)

Background: There is a gap between the number of patients waiting for a transplant and the number of kidneys available. Some kidneys from less-than-ideal donors are currently discarded, as medical teams fear that these organs will experience suboptimal graft survival. However, these organs could provide an acceptable therapeutic option if they were allocated for pre-emptive kidney transplantation in elderly candidates. This project aims to gather patients' perspectives on the ethical issues related to allocating less-than-ideal kidneys for pre-emptive kidney transplantation in elderly patients.

Methods: We conducted 14 semi-structured interviews with patients over 64 years of age with stage 4–5 chronic kidney disease and followed at the CHUM nephrology clinic.

Results: Most participants were in favour of using kidneys from less-than-ideal donors as a means to increase their access to transplantation, improve their quality of life, enable accelerated transplantation and avoid dialysis. Patients also wanted to be engaged in the decision-making process, underlining the importance of informed consent. Although the use of less-than-ideal kidneys offers the hope of returning to "normal" life, some patients were concerned about the risk of reduced graft survival and the need for a subsequent kidney transplant. In these cases, patients were interested in using mitigation strategies, such as prioritization for kidney transplantation from standard donors in the event of early graft loss associated with receiving less-than-ideal kidneys. They also recommended the development of a separate waitlist for patients consenting to pre-emptive transplantation with less-than-ideal kidneys.

Conclusion: The use of less-than-ideal donor kidneys for pre-emptive kidney transplantation appears to be an interesting option for elderly kidney transplant candidates. However, patient information and participation in the decision-making process are essential. Moreover, organ donation organizations and transplant programs should develop a separate waitlist for transplant candidates who have pre-consented to receive organ offers from less-than-ideal kidney donors.

ID#73

Title: Intraoperative hypotension during critical phases of liver transplantation influences acute kidney injury: a retrospective cohort study

Matthanja Matthanja - University Health Network

Introduction

Acute Kidney Injury (AKI) after orthotopic liver transplantation (OLT) occurs frequently and is associated with prolonged ICU and hospital stay, increased risk of chronic renal disease, and decreased graft survival. Intraoperative hypotension is associated with postoperative AKI and is a potential modifiable risk factor. We aimed to determine in which phase of surgery hypotension has the strongest association with AKI: the anhepatic or neohepatic phase.

Methods

This was a retrospective cohort study in adult patients undergoing OLT (2016-2022). Exclusion criteria were combined transplant, death or re-transplantation within 48 hours. Primary outcome was AKI defined as the Kidney Disease Improving Global Outcomes criteria. The exposure was hypotension and mean arterial pressure (MAP) was evaluated (in minutes) during the total duration of transplantation, the anhepatic and neohepatic phase. Multivariable logistic regression analysis was used to explore the association between intraoperative MAP and postoperative AKI.

Results

The etiology of liver disease of 1,259 patients was HCC (39%), Alcoholic Cirrhosis (21%), non-alcoholic steatohepatitis (20%) and Hepatitis C (20%). Median age was 58 years, median MELD-NA score was 19 (SD12-29) and 34% was living-related donation. Classic caval interposition was used in 74% and full caval clamp in 80% of cases. Median blood loss was 2.5L (SD1.5-4.1). AKI occurred in 577 patients (46%). MAP 20 minutes was associated with AKI (OR2.3, 95% CI 1.3-4.1), and during the an-hepatic phase at MAP 20 minutes (OR1.5, 95% CI 1.0-2.3) which became stronger at MAP 20 minutes (OR2.4, 95% CI 1.2-5.2). Confounder was etiology of acute hepatic failure.

Conclusion

Intraoperative hypotension is independently associated with AKI following liver transplantation. This association is mainly due to hypotension during the an-hepatic phase and not the neohepatic phase. Additional hemodynamic support should be considered in the an-hepatic phase to optimize postoperative kidney function.

ID#74

Title: Biological sex modulates the effects of the immunoregulatory fibrinogen-like protein 2 molecule on alloimmunity

Christina Lam - University Health Network

Introduction: The effects of sex differences in solid organ transplantation remain poorly understood. Females tend to mount more robust immune responses compared to males due to estrogen in the former and androgen in the latter. The immunoregulatory fibrinogen-like protein 2 (fgl2) molecule, expressed by regulatory T cells, holds potential as tolerizing therapy. Here, we hypothesized that fgl2's effect on allograft response is sex dependent.

Method: We first isolated T cells from male and female fgl2+/+ and fgl2-/- mice and measured their proliferation in vitro. We then intravenously injected either fgl2+/+ or fgl2-/- T cells into Rag-/- (fgl2+/+) mice (C57BL/6J background; H-2b) and gave them skin grafts from Balb/c donors (H-2d) after 24 hours (Fig 1a). The sexes of Rag-/- recipients and Balb/c donors were matched to the T cells. Dressings were removed 7 days post-transplant and grafts were monitored for up to 90 days (Fig. 1a).

Results: T cell-intrinsic fgl2 expression inhibited CD4+ T cell proliferation in vitro, but only in male T cells (Fig 1b). In contrast, while female CD8+ T cells tended to proliferate less than male T cells, T cell-intrinsic fgl2 did not have a strong effect on their proliferation (Fig. 1b). In the adoptive transfer experiment, fgl2 expression by the T cells did not affect graft rejection; however, female T cells rejected Balb/c grafts faster than male T cells (Fig 2a-b). In keeping with the in vitro data suggesting that male but not female CD4+ T cells can be regulated by fgl2, this observation suggests that T cell extrinsic fgl2 in the Rag-/- environment may have contributed to slowing graft rejection mediated by male T cells.

Conclusion: Our data reveal that fgl2 exerts its influence on allograft rejection in a sex-dependent manner and suggest that T cell-extrinsic sources of fgl2 can contribute to T cell regulation.

ID#75

Title: Loss, grief, failure in transplantation and the role of an arts-based intervention: A qualitative study with transplant patients

Marie-Chantal Fortin - Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM)

Background. Organ transplantation is often portrayed as a positive experience. However, data on patient perspectives regarding difficult moments throughout their transplant journey is sparse. While arts-based interventions have been shown to have a positive impact on patients' overall wellbeing, there is no data on their potential impact among solid organ transplant recipients. The objective of this exploratory study was to gather transplant patients' perspectives on the feeling of loss, grief and failure in transplantation and the potential role of arts-based interventions in coping with these difficult feelings.

Methods. Ten semi-directed interviews were conducted with organ transplant recipients from the CHUM between January and May 2024.

Results. Four lung, four liver and two kidney transplant recipients participated in the study. Physical difficulties associated with the loss of health and the physical challenges following their transplantation were participants' most frequently reported difficult moments. They also reported losing a sense of self, due to both the presence of the graft and the grief over aspects of life that are incompatible with being an organ recipient. For instance, they reported mourning previous life habits, like eating a certain type of food, that were now inappropriate for their post-transplant life. Although most participants had never participated in arts-based interventions themselves, the majority saw art as an activity that would allow them to escape their reality and express themselves. They thought such interventions should include different arts media, like visual art and literature. Most deemed the sharing aspect of their creation to be a key part of a successful arts-based intervention.

Conclusion. Participants were enthusiastic regarding the idea of an arts-based intervention to share difficult moments throughout their transplantation journey. Further participatory research with transplant patients and caregivers is warranted to clarify their expectations and eventually develop arts-based interventions that suit their needs.

ID#76

Title: Kidney perfusion fluid extracellular vesicles have a specific miRNA signature and affect Treg frequency in transplant rejection

Alissa Rutman - McGill University Health Centre

BACKGROUND: Machine perfusion of kidneys prior to transplantation has emerged as a technique to improve graft quality and can provide opportunities to assess the graft non-invasively prior to transplantation. This could improve allocation and tailor recipient management. Our group showed that kidneys under machine perfusion release HLA and miRNA containing extracellular vesicles (EV) which could serve as predictors of delayed graft function. Here, we aim to determine whether miRNA content of, and T-cell responses to kidney perfusion fluid EV (KP-EV) could predict graft outcomes such as transplant rejection.

METHODS: Perfusion fluid samples (n=19) were collected from deceased donor kidneys placed on the LifePort device following completion of perfusion. KP-EV were purified by sequential centrifugation. KP-EV were profiled by miRNA sequencing (HiSeq 4000). KP-EV from donors were co-cultured with PBMC from healthy controls. T cell activation was measured by flow cytometry. Clinical outcomes were recorded in our programmatic database over a 2 year period (n=4 graft rejection, n=15 stable grafts). T-tests and ANOVAs were used for statistical analyses.

RESULTS: miRNA sequencing of KP-EV revealed several miRNA to be upregulated (miR-193, miR-365, miR-193) or downregulated (miR-204, miR-338, miR-874, miR-1260) in KP-EV of donors of recipients with transplant rejection. KP-EV from kidneys whose recipients went on to experience rejection increased T-regulatory cells (CD4+CD25hiCD127loFoxP3+) in third party PBMC to a greater degree than those from kidneys whose recipients with stable grafts.

CONCLUSIONS: We demonstrate that KP-EV released by kidneys under machine perfusion contain miRNA that may serve as non-invasive pre-transplant markers to predict rejection. It is plausible that donor kidneys whose recipients have stable grafts produce less immunogenic EV, capable of inducing higher percentages of Treg, leading to improved graft function and tolerance. Further characterization of KP-EV may help in developing markers to assess graft quality, predict transplant outcomes and lead to novel therapies.

ID#77

Title: COVID-19 vaccination refusal and access to transplantation: An ethical conundrum. A qualitative study with key stakeholders

Marie-Chantal Fortin - Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM)

Background

Given the stronger immunological effects of vaccines pre-transplant, the issue of whether or not COVID-19 vaccination pre-transplant should be mandatory has been raised. The objective of this study was to gather transplant patients' perspectives on the ethical issues related to the vaccine mandate and access to transplantation.

Methods

We conducted semi-structured interviews with 50 patients (lung, liver, kidney and heart transplant recipients or patients waiting for a transplant). The interviews were digitally recorded and transcribed. Thematic and content analysis was conducted.

Results

Patients identified positive arguments for mandatory COVID-19 vaccination pre-transplant. In the context of an organ transplant, where resources are limited, many patients felt that the healthcare system has a duty to select recipients based on certain criteria and to maximize the chances of the transplant's success. Most of the patients interviewed also felt that transplant recipients have an obligation to take care of their health and to lower the risks of rejection of their transplanted organ. This is linked to the idea raised by many patients interviewed, who perceived vaccination in the context of transplantation as an act of respect for others—be they other potential recipients on the list, the donor or the donor's family, or the other vulnerable members of society. However, many of them preferred the idea of making vaccination a prioritization criterion rather than a discriminatory one. Lastly, some patients interviewed recommended that doctors present a vaccination mandate to patients, while others preferred that a nurse or another patient do it. All agreed on presenting a vaccination mandate at the very beginning of the transplantation process.

Conclusion

This study documents transplant patients' perspectives on mandatory COVID-19 vaccination pre-transplant. The findings can help in the implementation of vaccination recommendations while taking into account the opinions and ideas of patients on this subject.

ID#78

Title: Advanced and Voucher Donation in Canada: Stakeholders' Perspectives on Ethical and Logistical Issues

Marie-Chantal Fortin - Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM)

Background: Kidney paired donation is a great advancement in living donor kidney transplantation (LDKT) but does not address chronological incompatibility. Advanced and voucher donation allows a kidney donor to donate at the most appropriate time for them and to receive vouchers that could be redeemed by a specified person in need of a kidney transplant in the future, if they are a suitable transplant candidate. Advanced and voucher donation raises numerous ethical issues. The objective of this study was to survey the transplant community about advanced and voucher donation.

Methods: We conducted an electronic survey with living kidney donors (LKDs), transplant candidates (TCs), kidney transplant recipients (KTRs) and transplant professionals (TPs) about advanced and voucher donation. We used multiple-choice questions, short forced-choice questions using 5-point Likert scales and open-ended questions.

Results: A total of 209 participants completed the survey (72 LKDs, 34 TCs, 22 KTRs and 81 TPs). 62.7% of participants agreed with advanced donation and 55.5% were in favour of voucher donation. The two major arguments supporting advanced donation were that advanced donation respects the personal choice of the donor (81.3%) and prioritizes the donor's needs (73.2%). 51.7% of participants supported voucher donation because it will encourage more people to be living donors. The most important factor that would influence participants to take part in advanced and voucher donation would be that their loved ones could benefit in the future from their donation (32%). However, the uncertainties related to advanced and voucher donation were viewed as a barrier to participation for 42.1% of participants.

Conclusion: Participants were open-minded about supporting advanced and voucher donation since it respects the donor's autonomy and it could increase the number of LDKTs. However, uncertainties and logistical issues are barriers that need to be addressed before implementing this type of living donation.

ID#79

Title: Retinoic Acid-Related Orphan Receptor C (RORC): the Nuclear receptor that straddles Chronic Rejection, Inflammation and Cancer

Sarita Negi - McGill University Health Centre

Background: Transplantation often triggers chronic inflammation linked to complications such as chronic rejection, interstitial fibrosis, and tubular atrophy, as well as obesity, type 2 diabetes and cancer. Current immunosuppression poorly controls type-3 immunity, mediated by cells expressing the transcription factor retinoic acid-related orphan receptor C (RORC), and produce cytokines like IL17A, IL21and IL22. We recently demonstrated that TF-S10, an inverse agonist targeting RORC, reduces Th17 activity and prolongs skin allograft survival in sensitized mice. However, RORC's role in cancers remains uncertain, so we aimed to investigate its significance in two deadly cancers: pancreatic ductal adenocarcinoma (PDAC) and triple-negative breast cancer (TNBC).

Methods: RORC expression was assessed in PDAC and TNBC cell lines and inhibited using siRNA and TF-S10. The anti-proliferative effect of RORC inhibition was measured using CellTiter-Glo and colony formation assays. The effect of RORC inhibition on the expression of markers for cancer stem-cell (SOX2, MYC, OCT3/4 and NANOG) and the immune checkpoint (PD-L1) was measured by QPCR. RNAseq was performed after RORC inhibition using siRNA or TF-S10. The efficacy of TF-S10 was assessed against tumor formation using immunocompromised NOD mice. PDAC or TNBC tumors were established in NOD mice, and mice were treated with 25 mg/kg of TF-S10 or vehicle for 10 days. Tumor volumes were measured every alternate day.

Results: All cell lines expressed RORC, and its inhibition resulted in reduced cell proliferation and colony formation. TF-S10 showed an IC(50) of ~28mM and revealed concentration-dependent inhibition of colony formation. RORC inhibition decreased expression of cancer stem cell markers while inducing PD-L1. RNAseq revealed the upregulation of inflammatory pathways and downregulation of cell-cycle pathways, and epithelial-mesenchymal transition pathways upon RORC inhibition. TF-S10 reduced tumor burden in both PDAC and TNBC models, indicating RORC's significant role in tumor growth.

Conclusion: These findings suggest that RORC inverse agonist may hold promise for treating chronic rejection in transplantation and potentially reducing cancer risk.

ID#80

Title: Investigating serum cytokine and metabolite profiles associated with graft survival in adult kidney transplant recipients

Amy Thachil - BC Children's Hospital Research Institute

Background: Cytokine and metabolite expression in the pre-transplant period provides insight into the immunological milieu into which kidney transplant engraftment will occur, and the predisposition towards tolerance and rejection mechanisms. Here, we characterized the pre-transplant serum cytokine and metabolite environments to identify patterns related to chronic rejection and graft loss in adult kidney transplant recipients.

Methods: Pre-transplant serum samples were assayed using a targeted panel to evaluate concentrations of 92 cytokines and inflammatory proteins. Quantitative mass spectrometry was used to detect concentrations of 630 unique metabolite analytes. A binary outcome of chronic rejection versus stable graft function was modelled by constructing partial least squares discriminant analysis (PLSDA) classifiers using cytokine and metabolomics data, separately. Individual cytokine and metabolite discriminant scores (dscores) were extracted to evaluate their combined predictive value and correlation.

Results: Serum samples were obtained from 120 adult kidney transplant recipients with stable graft function at 8 years post-transplant (n=83, controls) or chronic rejection (cellular, antibody or mixed) and graft loss within 5 years of transplant (n=37, cases) (Table 1). The primary cytokine PLSDA classifier was optimized at 5 principal components derived from measurements of 10 cytokines: MCP.3, IL-17A, CXCL11, OSM, MCP.4, FGF.23, FGF.21, CXCL5, IFN-g and NRTN (training AUROC=0.80, 95% CI: 0.71-0.88, LOOCV AUROC=0.69, 95% CI: 0.59-0.79). The optimal metabolite classifier contained 5 principal components consisting of measurements from 30 metabolites (training AUROC=0.94, 95% CI: 0.89-0.98, LOOCV AUROC=0.82, 95% CI: 0.74-0.90). Cytokine and metabolite dscores produced an AUROC of 0.97 (95% CI: 0.95-1.00) (LOOCV AUROC=0.97, 95% CI: 0.93-1.00) when combined, and showed a modest, positive association (Spearman’s Rho=0.25, p=0.006) (Figure 2).

Conclusion: This study provides evidence of pre-transplant serum cytokine and metabolite patterns associated with chronic rejection and graft loss in kidney transplantation. Combined cytokine and metabolite profiling may improve predictive performance compared to either platform alone.

ID#81

Title: Impact of Treating Asymptomatic Bacteriuria Immediately After a Kidney Transplant: A Retrospective study

Elyse Potvin - University of Alberta

Context:

Following kidney transplant (KT), there is a high rate of asymptomatic bacteriuria (AB) despite no symptoms of urinary tract infection (UTI). KT recipients are at risk of UTI so a dilemma to treat AB as a preventive measure exists. Guidelines recommend against screening or treating AB more than 1-2 months after KT but are unable to give recommendations for the first month due to lack of data.

Methods:

Retrospective review of adult KT charts from a single center, from November 2019 to March 2021. We assessed urine culture results and how AB was managed in the first 2 months post KT. The rate of UTI, hospitalizations, kidney function and rejection at 2-year follow-up were analyzed to determine if treated AB affects outcomes.

Results:

101 KT patients were included, male to female ratio of 2:1 and mean age of 51 (SD 12.8). 64.4% were from deceased donors, 89% first-time transplant recipient. Induction treatment was Thymoglobulin or Basiliximab (15% vs 85%). Mean duration of urethral catheterization 5.9 days (SD 2.07) and 42.3 days (SD 26.51) for ureteral stent. During the first 2 months, 74/101 (73.26%) patients developed positive urine cultures, and 12 (16.2%) had UTI. Of 62 AB, 24 (38.7%) received antibiotics.

After 2 years of follow-up, the rate of UTI affecting treated AB was 38%, while the rate of UTI after untreated AB was 13%, and those without any early positive urine culture was 15%. Furthermore, having a symptomatic UTI within the first 2 months lead to a 50% risk of UTI within 2 yr. ($P = 0.014$).

Conclusion:

These preliminary data raise concern that treating AB early post transplant may paradoxically increase the number of UTI at 24 months. Further prospective study is required.

ID#82

Title: Stratifying risk of antibody-mediated rejection in kidney transplant recipients by molecular compatibility strategy: a retrospective nested case-control study

Edden Gitelman - McGill University

Background: Molecular incompatibility is associated with immune injury in kidney transplant recipients (KTR). Eplets are configurations of polymorphic amino acid residues on the HLA surface capable of determining antibody specificity. Eplet mismatches (EMMs) occur when donor eplets absent from the recipient's repertoire are introduced following transplantation. We aimed to characterize EMM subsets as determinants of antibody-mediated rejection (AMR), and to inform a threshold of EMM load beyond which risk is more pronounced.

Methods: We conducted a nested case-control study from a retrospective multicenter cohort of first-time kidney-only transplant recipients. Cases (N = 98) were recipients with AMR across its continuum. Controls were randomly selected from the remaining cohort, matched on centre, transplant year, donor type, and time post-transplant. EMMs were estimated from HLA genotyping by Next Generation Sequencing (NGS). We fit sequentially nested multivariable conditional logistic regression models adjusting for recipient, donor and transplant characteristics to assess the risk of AMR as a function of molecular compatibility strategy (by HLA class and antibody-verification status). We also applied a restricted cubic spline transformation to ascertain an EMM load threshold beyond which risk is more pronounced.

Results: Unadjusted conditional logistic regression models yielded odds ratios (OR) and 95% confidence intervals (95% CI) for AMR estimated at 1.04 (1.01, 1.06), 1.10 (1.03, 1.17), and 1.12 (1.04, 1.2), while multivariable models adjusting for recipient age, sex, induction agent and time-varying mycophenolate dose yielded ORs of 1.04 (1.01, 1.06), 1.11 (1.04 1.18) and 1.12 (1.04, 1.21) for each additional HLA class II, antibody-verified (AbVer) class II, and Leiden AbVer class II EMMs, respectively. A restricted cubic spline transformation suggested that the risk of AMR was more pronounced beyond a threshold of ≥5 class II Leiden AbVer EMMs.

Conclusion: Ensuring donor/recipient compatibility on HLA class II Leiden AbVer eplets could help mitigate risk of AMR.

ID#83

Title: Metabolic dysfunction-associated steatotic liver disease is associated with worse outcomes in kidney transplant recipients

Christina Yoon - McGill University

Background: The hepatic manifestation of metabolic syndrome, metabolic dysfunction-associated steatotic liver disease (MASLD), is considered a risk factor for cardiovascular disease and chronic kidney disease. Given the implications of MASLD in kidney transplant recipients (KTRs) are not well defined, we sought to investigate its association with graft and patient outcomes.

Methods: We conducted a retrospective cohort study in first-time KTRs (2008-2020) and assessed the association between time-varying and time-fixed MASLD (defined as hepatic steatosis detected by abdominal ultrasound and ≥ 1 adult cardiometabolic criteria) with a composite endpoint of advanced graft dysfunction (defined as eGFR < 3 0 mL/min/1.73m2 sustained for ≥3 months), death censored graft failure (DCGF, defined as return to dialysis or re-transplantation), and death with graft function (DWGF). We fit sequentially nested Cox proportional hazards models adjusted for recipient (sex, age), donor (sex, type (living/deceased)), and transplant (cold ischemia time, era, induction, and maintenance immunosuppression) characteristics. Multivariable models were also fitted for graft dysfunction, DCGF, and DWGF endpoints.

Results: Among 650 eligible KTRs, we observed 120, 88, 100, and 237 allograft dysfunction, DCGF, DWGF, and composite endpoints, respectively, over a median follow-up of 4.5 years. Unadjusted models demonstrated that time-varying MASLD was associated with an increased risk of the composite endpoint (hazards ratio (HR) 1.42 (95% confidence interval 1.09, 1.84)), graft dysfunction (1.49 (1.03, 2.15)), DCGF (1.19 (0.77, 1.83)), and DWGF (1.4 (0.94, 2.09)). Multivariable models yielded HRs of 1.26 (0.97, 1.64), 1.24 (0.86, 1.78), 1.15 (0.75, 1.78), and 1.56 (1.04, 2.33) as a function of time-varying MASLD for the same endpoints, respectively. Time-fixed analyses generated similar trends.

Conclusions: The presence of MASLD is associated with increased mortality in KTRs. Monitoring for MASLD in transplant candidates and KTRs may help identify patients who could benefit from interventions to mitigate risks and complications of MASLD, ultimately improving survival of KTRs.

ID#84

Title: Normothermic regional perfusion: the Canadian landscape

Xin Yu Yang - Université de Montréal

Background: Normothermic regional perfusion (NRP) has been used to improve graft viability after controlled donation after circulatory death (cDCD). It has shown promising results in many other countries. This article reviews the surgical techniques of NRP and the barriers to its implementation within the Canadian organ transplantation landscape.

Methods: NRP involves restoration of the in-situ organ perfusion using extracorporeal membrane oxygenation after determination of death. In abdominal NRP, the extracorporeal circuit is connected via cannulas into the iliac vessels or the abdominal aorta and inferior vena cava. The supra celiac aorta is occluded to prevent reperfusion of the brain. In thoracoabdominal NRP, the aortic arch vessels are occluded to prevent brain reperfusion.

Results: The 2023 Canadian clinical practice guideline published a unified brain-based definition of death after arrest of circulatory or neurological function: Death is defined as the permanent cessation of brain function. Given this, restoration of circulatory perfusion for organ procurement is not in violation of the dead donor rule as long as the absence of brain perfusion is maintained.

NRP improves the selection of grafts through a continuous in vivo assessment of organ viability. In liver transplantation, macro-and microscopic appearance, bile production and biochemical factors are assessed. Evidence has shown that NRP leads to a significantly decreased risk of ischemic cholangiopathy and liver graft failure compared to conventional cDCD organ recovery. Kidney viability is evaluated based on macroscopic aspects and urine production. Renal allograft recovered by NRP has proven to yield superior graft function compared to non-NRP recovery with lower rates of delayed graft function.

Conclusion: The implementation of NRP in Canada holds great potential to improve transplant outcomes and reduce organ shortages. Successful integration of NRP into clinical practice necessitates collaboration among all stakeholders to establish standardized protocols within the Canadian medical, ethical, and legal framework.

ID#85

Title: An Algorithm for Evaluating Kidney Transplant Wait Times

Anastasiya Basanets - Polytechnique Montreal

Patients who are listed for a kidney transplantation often report anxiety with regards to uncertainty of expected wait time to transplantation. As kidney allocation in the province of Quebec is driven by a score, we hypothesize that personalized estimates of expected wait time to kidney transplant offers can be provided to kidney transplant candidates. Our aim was to develop a model that provides personalized estimates of wait time to and average quality of future offers for kidney transplant candidates.

We performed a retrospective cohort study using data from Transplant Québec. All donors from whom at least 1 kidney was transplanted on the score-based list were included in the study between 2014 and 2018. The allocation score gives points for candidate time on dialysis, cPRA, age, and donor/ candidate DR and age matching. All candidates registered during that period were also included. Candidates' wait time was modeled by a marked Poisson process. We estimated donor quality using the Kidney Donor Profile Index (KDPI) with 2023 as the reference year. The quality of the offer was modeled by a continuous probability distribution, which constitutes the mark of this process.

The study cohort comprised 840 unique donors. Using the model, we determined wait time before receiving an offer at any given time and average quality of future offers. These depend on the candidate and donor characteristics that are used in the allocation score at the time a prediction needs to be made. Figure 1 provides examples of wait time to offer estimations for 4 different patients, with the solid circle showing the observed time to offer (ground truth). Table 1 provides, for the same 4 patients, estimates of time (in months) required to receive an offer from a donor who does not have a high KDPI (KDPI≤83%).

Our model helps improving the way the transplant team can inform kidney transplant candidates as to expected wait time of kidney offers.

ID#86

Title: Assessing obesity and diabetes mellitus status in measuring kidney transplant outcomes in female transplant recipient with obesity

Roxaneh Zaminpeyma - Dallhousie University

Background: Obesity can be associated with adverse outcomes post-kidney transplant (KT). Whether the risk associated with obesity and/or diabetes mellitus (DM), an associated comorbidity, is influenced by patient sex is unknown. Therefore, we aimed to assess the association between elevated body mass index (BMI) in patients with versus without DM at KT, and post-KT outcomes, and whether this risk was modified by patient sex.

Methods: In a cohort of adult KT recipients in the U.S. (SRTR 2000-2017), we examined risk associated with combined obesity (BMI ≥ 30 kg/m2) and DM status as a nested variable (i. non-obese/no DM (reference); ii. non-obese/DM, iii. obese/no DM, iv. obese/DM). We used multivariable cox proportional hazards and logistic regression models to examine the risk of death censored graft loss (DCGL) and all cause graft loss (ACGL) overall and in sex stratified analyses. Effect modification of DM and obesity by patient sex was assessed for each outcome.

Results: A total of 221,925 recipients were included in the study. The overall risk of both DCGL and ACGL was highest in combined obesity/DM, (aHR 1.33, 95% CI 1.26-1.41 and aHR 1.35, 95% CI 1.30-1.40, respectively). The risk of both DCGL and ACGL was significantly higher in combined obesity/DM for females (aHR 1.48, 95% CI 1.36-1.61; aHR 1.44, 95% CI 1.36-1.52, respectively) than males (aHR 1.24, 95% CI 1.16-1.33; aHR 1.27, 95% CI 1.21-1.32, respectively), Figure 1 and 2. Recipient sex modified the association between DM and both ACGL and DCGL (p-value < 0.001 for each), but did not modify the association between obesity and either outcome.

Conclusion: Combined obesity/DM was associated with increased risk of both DCGL and ACGL; this risk was significantly higher in females than males. Patient sex modified the association between DM and both DCGL and ACGL, but not association between obesity and ACGL.

ID#87

Title: LGALS1 knockdown in human glomerular microvascular endothelial cells preserves response to IFNg and reveals a proteome similar to that seen in biopsies with antibody-mediated rejection

Alex Boshart - University Health Network

Background: Antibody-mediated rejection (AMR) accounts for >50% of premature kidney graft loss. AMR is caused by donor specific antibodies (DSA) against human leukocyte antigens (HLA) on the graft. DSA binding to HLA triggers endothelial damage via complement activation, immune cell activation, and release of cytokine IFNg, yet novel therapeutic targets are needed. We identified an immunomodulatory protein LGALS1 that was significantly increased in endothelial cells in AMR glomeruli. To investigate the role of LGALS1 in AMR, we conducted LGALS1 knockdown in primary human glomerular microvascular endothelial cells (GMECs) in vitro and assessed the proteome-wide changes following IFNg treatment.

Methods: GMECs were exposed to IFNg (500 U/mL) or vehicle for 24h. Immunoblotting assessed HLA class-II DP expression. LGALS1 knockdown was achieved via electroporation with 100 nM anti-LGALS1 siRNA or scramble control, with knockdown efficiency evaluated at the gene and protein levels. Subsequently, IFNg or vehicle treatment was administered for 24h. Proteome analysis of GMECs was then performed using LC-MS/MS on Q-Exactive mass spectrometer.

Results: HLA class-II DP was induced in IFNg-stimulated GMECs but was absent in vehicle-treated cells (Fig.1A). siRNA-mediated knock-down decreased LGALS1 gene expression in GMECs at 48h, 72h, and 96h (Fig.1B) and protein expression at 72h (Fig.1C). Proteome analysis showed a strong IFNg response and a decrease in extra cellular matrix (ECM) proteins, regardless of the siRNA treatment group. LGALS1 protein was decreased by siRNA treatment, and we identified two groups of metabolic proteins that were significantly altered by LGALS1 siRNA (Fig.1D).

Conclusion: LGALS1 was successfully knocked down in GMECs. IFNg treatment of GMECs in vitro recapitulates AMR proteome seen in patients' biopsies, exemplified by up-regulation of immune response proteins and down-regulation in ECM related proteins. Our next step is to add more replicates and examine IFNg signalling, using phosphoproteomics, in GMECs in the presence or absence of LGALS1.

ID#88

Title: The therapeutic potential of targeting nuclear receptor retinoic acid-related orphan receptor gamma (RORγ) in hepatocellular carcinoma

Sabrina Leo - McGill University Health Center Research Institute

Hepatocellular carcinoma (HCC) primarily arises through inflammation-associated etiologic factors that lead to liver cirrhosis. Type 3 immunity which is characterized by cells that produce the pro-inflammatory IL-17A cytokine, which is modulated by the master transcriptional factor retinoid acid-related orphan receptor gamma (RORγ), plays a significant role in acute and chronic allograft rejection. Moreover, over-expression of the cytokine and its transcription factor are implicated in inflammatory pathways that lead to metabolic syndrome, cirrhosis and the development of several cancers, including cirrhosis-induced HCC. Currently, liver transplantation is the most effective therapy for HCC. Advanced disease, however, is a contradiction due to the risk of recurrence. We investigate what cell properties are affected when RORγ is targeted.

Human HCC cell line HuH-7 and mouse HCC cell lines Hepa1-6 and Hep55-1.c were used. RORγ-targeting silencing RNA (siRORC) sequences were designed and a novel RORγ inverse agonist (C#10) generated at the RI-MUHC were used to inhibit RORγ activity. The assays used to test the effects of siRORC and C#10 inhibition in HCC cells include cell viability assays, colony formation assays, cell proliferation assays, RT-qPCR, immunofluorescence microscopy and western blot.

HCC cell lines HuH-7, Hep-55.1c and Hepa1-6 highly express RORγ. Cell viability, colony formation and cell proliferation rates were decreased significantly with siRORC or inverse agonist C#10 treatment. RORγ inhibition increased PD-L1 expression in the HCC cells and decreased cancer stem cell markers.

To conclude, human and mouse HCC cells highly express RORγ. Targeting RORγ with siRORC or RORγ inverse agonist C#10 suppressed cell viability, cell proliferation, cancer stem cell markers and colony formation of all three cell lines, while PD-L1 expression was increased. This data suggests that RORγ is a potential target for HCC and may have the dual benefit of preventing allograft rejection and HCC recurrence after liver transplantation.

ID#89

Title: Exploring the Impact of the Median Meld at Transplant Minus 3 (MMaT-3) Exception Points System on Waitlist Mortality for Liver Transplant Patients in Atlantic Canada

Panthea Pouramin - Dalhousie University

Background: Globally, liver transplant (LT) recipients are prioritized based on the risk of waitlist mortality using the Model of End-Stage Liver Disease (MELD). Given their low MLED scores, Hepatocellular Carcinoma (HCC) patients have traditionally been allocated exception points to compete with non-HCC patients. However, historically these exception points have overprioritized HCC patients. To more fairly allocate livers, the Median Meld at Transplant minus 3 (MMaT-3) scoring system was adopted. MMaT3 assigns reflective exception points based on the previous year's patient MELD scores at transplant. We aimed to assess the impact of MMaT3 adoption on waitlist mortality and transplantation rates amongst HCC and non-HCC patients.

Methods: A retrospective chart review of patients who were listed for a LT between 2015-2023 in Atlantic Canada was conducted. Waitlist mortality and transplantation rates were compared pre MMaT-3 and post- MMaT-3 implementation.

Results: 240 patients (143 pre- vs. 97 post-MMaT-3) were included. Post-MMaT3, non-HCC patients were significantly more likely to receive a LT (67.0% vs. 84.4%; p = 0.014) and experienced less waitlist mortality 1-year post-listing (27.8% vs. 14.1%; p=0.04), pre- and post-MMaT-3. There was no change in transplant rate (93.5% vs. 81.8%; p=0.11), or 1-year mortality (6.5% vs. 18.2%; p=0.11), among HCC patients. In multivariate cox regression, after correcting for Natural MELD score, age, and BMI, the introduction of MMaT-3 increased the probability for non-HCC patients to receive a transplant (HR: 1.69, [1.15, 2.49]; p < 0 .008). Yet, there was no change in the time for receiving a transplant post MMaT-3 in HCC patients (HR: 1.02 [0.61, 1.72]; p=0.94).

Conclusion: Our study demonstrated that implementing the MMaT-3 exception system decreased waitlist mortality of non-HCC patients with no discernable impact on outcomes for HCC patients listed for a transplant in Atlantic Canada.

ID#90

Title: Patterns of BK viremia and clinical outcomes in kidney transplant patients in British Columbia

Ross Doyle - University of British Columbia

Background

BK viremia and nephropathy after kidney transplant represent clinical challenges without satisfactory therapy, risking allograft loss, through virus-associated nephropathy and rejection. Detailed descriptions of viremia patterns and kinetics are lacking, preventing development of robust surrogate endpoints in clinical trial design. We sought to describe viremia and outcomes in kidney transplant recipients in British Columbia (BC).

Methods

We examined all BK virus laboratory assessments in BC between 2010-2023. Patterns of viremia in kidney transplant recipients were individually classified based on the peak level and outcome of viremia. Intra- and inter-rater agreement was determined. We evaluated the outcomes for these patients.

Results

BK measurements were performed on 4721 patients. Most (3273, 69.3%) never developed detectable viremia. Of 1448 patients who developed detectable viremia, four patterns of peak viremia and three patterns of outcomes of viremia were defined (Figure 1). Intra-rater agreement was high (94%) and among 12 physicians, blinded to pattern assignment, inter-rater agreement was substantial (Fleiss kappa 0.73, p 100,000 copies) and sustained viremia patterns were associated with greater death censored graft loss compared to patients who followed other patterns (Figures 2 & 3). eGFR declined fastest in those patients with very high peak compared to other groups (median -1.2 compared to -0.1 to -0.2 ml/min/1.73m2/year in other groups).

Conclusion

We identified patterns of peak viremia and outcomes of viremia in a large cohort of kidney transplant patients, managed with contemporary immunosuppressive protocols. These were reproducibly defined by different physicians. Most patients who develop detectable BK viremia have ongoing persistent/intermittently detectable viremia. Graft failure was more common among patients whose peak was classified as very high and whose outcome was classified as sustained viremia.

ID#91

Title: Defining optimal cryopreservation conditions to develop an improved regulatory T cell cryopreservation protocol for tolerogenic cell therapy in transplantation

Sarjana Alam - University of Alberta

Background

Regulatory T cell (Treg) tolerogenic therapy is a promising innovation for preventing transplant rejection. Defining optimal Treg cryopreservation conditions would augment successful clinical implementation. The currently used cryoprotectant agent (CPA) dimethyl sulfoxide (DMSO) is cytotoxic, contributing to poor Treg recovery and function post-thaw. CPAs such as ice recrystallization inhibitors (IRIs) or dextran may offer lower toxicity and greater cryoprotection. Here, we assessed toxicity of various CPA conditions and ability to improve post-thaw Treg viability and function.

Methods

Tregs were isolated from peripheral blood of healthy volunteers (n=3) or thymus tissue obtained during pediatric cardiac surgeries (n=2) and expanded in culture using our established protocols. After expansion, cells were suspended in: 1) base solution, 2) 10% DMSO (standard protocol), 3) 5% DMSO, 4) 5% DMSO with IRI, and 5) 5% DMSO with 5% dextran for up to four hours at 4oC, 22 oC and 37oC. Aliquots of each cell suspension were cryopreserved, thawed, and cultured. Recovery and viability were assessed by an automated cell counter, and phenotype by flow cytometry.

Results

88-94% of cells were CD4+CD25+FOXP3+, maintaining Treg phenotype throughout expansion and after cryopreservation. Treg recovery substantially decreased when exposed to 10% DMSO at 37 °C (median recovery: 27% at 2 h and 4% at 4 h) compared to all other conditions (> 92% at 2 h and > 88% at 4 h) (Figure 1). No clear viability differences were observed between cells exposed to 5% DMSO alone, with IRI, or with dextran (n=5). Post-thaw culture experiments' preliminary results did not show clear differences in Treg viability or quantity between different CPA conditions (n=2).

Conclusion

Decreased DMSO concentration may be key to reducing CPA toxicity to Tregs. Identifying the optimal CPA condition for Tregs will significantly advance development of an optimal cryopreservation protocol for therapeutic Tregs.

ID#92

Title: Gastrointestinal Viral Infection in Adult and Pediatric Solid Organ Transplant Recipient: A Retrospective, Single-center Study from 2015 to 2022

Dima Kabbani - University of Alberta

Background: Gastrointestinal (GI) viruses are common causes of diarrhea in solid organ transplant recipients (SOT). Little is known of the difference in epidemiology, clinical presentation, and possible complications of gastrointestinal viruses between adult (A) and pediatric (P) solid organ transplant recipients.

Methods: This is a single-center retrospective study of pediatric

Results: During the study period, out of 5621 SOT, 871 (P:15%) SOT had at least 1 GVP, and 192 (22%) tested positive for at least 1 virus. (figure 1). 177 SOT had 1 GI virus/GVP and 15 at least 2 viruses/GVP. Pediatrics were more likely to have positive GVP (P:48.6% vs A:16.5%), multiple viruses per GVP (P:18.1% vs A:1.7%), and multiple different viruses during follow-up period (P:26.3% vs A:2.5%) (Table 1) .NoV was the most common single virus in A (69.2%) and P (26.4%) followed by SaP (A:14.2%, P13.9%). Chronic diarrhea (more than 14 days) was common in SOT with SaP (A:76%, P:70%), NoV (A:65.1%, P:42.1%), and Adv (A:47.2%, P:50%). NoV was associated with acute renal failure in (A:80.7%, P:36.8%), weight loss (A:47%, P:31%), and hospitalization (A:41%, P:26.3%). Treatment for NoV included antimotility drugs (A:77.1%, P:21.1%), oral immunoglobulin (A:37.3%, P:0), Nitazoxanide (A:9.6%, P:5.3%), and modification of immunosuppression (A:36.2%, P:10.5%).

Conclusion: Although NoV is the most common cause of GI viral infection in SOT, P-SOT had more diverse and mixed GI viral infections. Chronic diarrhea, weight loss, and modification in immunosuppression are common with NoV.

Further studies are needed to assess the outcomes of GI viruses in SOT.

ID#93

Title: Long Term Outcomes of Kidney Transplant Recipients from the Canadian Highly Sensitized Patient Registry

Rahul Mainra - University of Saskatchewan

Background: Sensitized patients with end stage kidney disease have reduced access to transplantation. The Canadian Highly Sensitized Program (HSP) was established to find immunologically compatible donors for sensitized waitlisted patients. Over 600 patients have been transplanted however long-term outcomes are unknown and with the upcoming launch of the Willing to Cross program it is critical to understand outcomes in sensitized recipients who have received an HLA-compatible transplant.

Methods: This is a retrospective analysis of waitlisted and kidney transplant recipients (KTR) within the HSP registry from 2013 to 2020. Data was obtained from the Canadian Transplant Registry. Baseline demographics, patient survival (PS), all-cause graft survival (ACGS) and death censored graft survival (DCGS) was calculated.

Results: 1788 patients were followed for a median follow-up of 4.8 years. Demographic data of transplanted and non-transplanted patients is presented in Table 1. Of the 676 KTR, 62.4% were female and mean age was 54.3 +/- 13.6 years. KTR received a median of 2 (IQR 1, 3) HSP offers prior to transplantation. The median wait time to transplant was 177.8 days (IQR 47.5-517.4). One year median serum creatinine and eGFR was 110 umol/L (IQR 88-148) and 54 ml/min (IQR 37-72), respectively. Rejection episodes occurred in 23% of patients with more T-cell mediated rejection compared to antibody mediated rejection, 61% vs. 16% and 23% had mixed rejection. Overall, PS was 77% (Figure 1A), ACGS was 73% (Figure 1B), DCGS was 93% (Figure 1C).

Conclusion: We present for the first-time long-term outcomes of KTR from the Canadian HSP registry. Patient and graft outcomes are excellent with acceptable rates of acute rejection. This data is reassuring and provides a benchmark as we implement a Willing to Cross program for very highly sensitized patients. Further granular data is required to understand the outcomes of non-transplant patients in the HSP registry.

ID#94

Title: The heart of innovation: Evaluating the Traferox cooler's impact on ischemic times and short-term heart transplant outcomes

Lebei Pi - Toronto General Hospital

BACKGROUND

Recent advancements in static controlled hypothermia technology have markedly enhanced donor heart preservation practices, particularly improving donor heart utilization and increasing ischemic times without compromising short-term outcomes. The Traferox X-Port Transport cooler (Traferox Technologies Inc., Toronto, ON) is a novel device that maintains donor hearts at a temperature range between 8 to 10^{0}C. We sought to describe our experience with the Traferox cooler in comparison to standard static cold storage (SCS).

METHODS

We conducted a single centre retrospective review of 20 consecutive heart transplants (HT) from 2023-2024 stratified by Traferox cooler (n=9) vs. SCS (n=11). The primary aim was to assess cumulative ischemic time and short-term recipient outcomes including severe primary graft dysfunction (PGD), length of stay (LOS), and dialysis requirement post-operatively. We summarized clinical characteristics using descriptive statistics. Between-group differences were compared using the Fisher's exact test, t-test and Mann-Whitney U tests, with a p-value < 0.05 as statistically significant.

RESULTS

Among 20 recipients included, there were no differences in donor age (32 vs. 33 years, p=0.47), recipient age (51 vs. 59 years, p=0.4), or number of recipients supported with a durable left ventricular assist device (LVAD) between Traferox vs. SCS groups (3 vs. 3, p=1.0) (Table 1). However, Traferox enabled significantly longer cumulative ischemic times (259 mins vs. 153 mins, p=0.001). There were no cases of severe PGD or mortality with either storage method. Additionally, there were no differences in LOS, 30-day readmission rates and transient dialysis requirement post-operatively. Within the Traferox group, the mean probe temperature was 8.58^{0}C (SD 1.05^{0}C), minimum probe temperature 6.74^{0}C (SD 2.06^{0}C), and maximum probe temperature 13.09^{0}C (SD 3.31^{0}C).

CONCLUSION The Traferox cooler facilitated longer ischemic times and greater distances traveled for organ procurement, without compromising short-term outcomes, demonstrating a potential advantage over SCS.

ID#95

Title: Pneumocystis pneumonia outcomes in solid organ transplant recipients: a population-based study over 20 years (2002-2022) in Ontario, Canada

Carson Lo - St. Joseph's Healthcare Hamilton

Background: While it is well established that HIV-positive and non-HIV immunocompromised patients are susceptible to Pneumocystis pneumonia (PCP), comparing PCP outcomes between patients with different underlying immunocompromising conditions is critically important to optimize chemoprophylaxis strategies.

Methods: In this population-based cohort, we determined contributing factors to 90-day all-cause mortality following PCP diagnosis among patients living with HIV (PLWH) and solid organ transplant recipients (SOTRs) hospitalized in Ontario, Canada between Apr/1/2002 and Dec/31/2022. We linked data from provincial health administrative databases using unique encoded identifiers and included all adult patients hospitalized with PCP based on diagnostic codes from hospital discharge abstracts. We used logistic regression models to estimate unadjusted and adjusted odds ratios (uOR and aOR) and 95% confidence intervals (95%CI) for the associations between underlying immunocompromising conditions and PCP outcomes.

Results: A total of 879 patients were hospitalized with PCP, including 121 SOTRs (13.7%) and 758 PLWH (86.2%). 90-day mortality rates were 19.8% in SOTRs and 13.2% in PLWH. In the unadjusted model, 90-day mortality was not significantly associated with organ transplantation (OR=1.58; 95%CI, 0.96-2.62) or HIV infection (OR=0.62; 95%CI, 0.38-1.03). Comparing HIV patients to liver SOTRs, liver SOTRs experienced higher mortality (uOR=8.54, 95%CI=3.11-23.46). In the adjusted model, liver transplantation was associated with an increased risk of 90-day mortality (aOR=4.36; 95%CI, 1.40-13.59). Among SOTRs, in the unadjusted analysis, liver transplant recipients had an increased risk of 90-day mortality (uOR=9.18; 95%CI, 3.00-28.09)

Conclusion: Among SOTRs, liver transplant recipients are at particularly higher risk of mortality following PCP diagnosis. Our findings may prompt a re-evaluation of current PCP prophylactic strategies in liver transplant patients.

ID#96

Title: A kidney transplant case involving donor-derived candidemia and infective endocarditis, further complicated by post-transplantation mucormycosis, is being considered for a kidney retransplantation.

Mohammad Reza Rahimi Shahmirzadi - Western University

Bacground: Transmission of donor-derived candida infections presenting significant health risks for the recipient and can compromise the transplanted kidney. The medical team is evaluating the feasibility of a kidney retransplantation, highlighting the need for rigorous infection control and innovative treatment strategies in managing post-transplant complications.

Case Report: A 46-year-old female patient with a history of diabetes and end-stage renal disease (ESRD) received a renal transplant from a deceased donor in September 2020. Shortly after the transplant, Candida Albicans was reported in a sputum culture from the donor, and subsequent blood and urine cultures also tested positive for Candida Albicans. Echocardiographic evaluations revealed a vegetation on her aortic valve, but cardiac surgery determined that no surgical intervention was necessary. Consequently, her caspofungin treatment was extended to six weeks, followed by lifelong prophylaxis with fluconazole. In December 2021, she developed sinusitis for which she was treated with antibiotic and nasal steroids. Unfortunately, the patient then developed a dental abscess, orbital cellulitis. She was subsequently treated empirically with piperacillin/tazobactam, vancomycin, and amphotericin B, followed by extensive sinus debridement and concomitantly, the immunosuppression was tapped due to the severity of infection. Histopathological examination and cultures confirmed mucormycosis. She was initially treated with AmBisome, later transitioning to isavuconazole. The active mucormycosis infection and subsequent cessation of immunosuppression led to the failure of her kidney transplant. In June 2023, the patient was evaluated for a second kidney transplant. The assessment indicated a high risk of mucormycosis reactivation with the resumption of immunosuppression. Recommendations included that she be maintained on isavuconazole prophylaxis for at least one-year post-transplant.

Conclusion: Managing kidney transplant recipients with complex medical backgrounds requires a multidisciplinary approach. Prompt intervention and vigilant monitoring are vital for addressing donor-derived infections and post-transplant complications. Balancing the degree of immunosuppression and infection prophylaxis in cases of severe fungal infections.

ID#97

Title: Systematic review on effect of donor-recipient size mismatch on kidney allograft outcomes

Sabaa Asif - University of Toronto

Background

Since the late 1990's, there have been concerns that the size mismatch between a larger recipient and smaller donor (or donor kidney), lead to worse allograft outcomes. Several studies have been conducted to assess this relationship but there is no published systematic review available that has summarized and synthesized this disparate literature.

Methods

A comprehensive search strategy was applied to studies published between January 1, 1946 to February 5, 2024. All studies evaluating adult kidney transplant recipients were included. Studies not in English, unavailable in full text, and those including donors less than 16 years of age were excluded. After removal of duplicates, titles and abstracts were screened and relevant studies underwent full text review by two independent assessors. After full text review, studies that fit the inclusion and exclusion criteria were analyzed. The findings were discussed and conflicts were resolved by a third reviewer. Risk of bias was assessed using the ROBINS-E tool.

Results

A total of 1377 studies were identified using the search strategy. After initial screening, removal of duplicates, and full text review, 56 studies were included in the final analysis. The studies showed significant heterogeneity in terms of the type of exposure used to classify size mismatch, exposure subgrouping, and/or outcomes assessed. Among the included studies, 32% demonstrated worse allograft outcomes with unfavorable size mismatch, while 11% showed no association. More than half of the studies (57%) showed mixed findings. All studies had high or very high risk of bias when examined using ROBINS-E tool.

Conclusion

Available studies do not provide strong evidence to support or reject the idea of nephron underdosing, however the quality of existing reports was generally poor. Rigorously designed and analyzed studies of this topic, with thoughtfully constructed exposure definitions, outcome assessments, confounder control, follow-up, and statistical analyses remain a priority.

ID#98

Title: NSAID Prescriptions in Living Kidney Donors

Mikayla Laube - University of Calgary

Background: Current guidelines recommend that living kidney donors should avoid non-steroidal anti-inflammatory drugs (NSAIDs) due to their potential nephrotoxic effects. It is unclear if physicians are adhering to this guideline recommendation.

Methods: We conducted a population-based, retrospective cohort study of adult living kidney donors in Alberta, Canada, who donated between 2002 and 2019. We identified the proportion of living kidney donors who filled an NSAID prescription at least 1-year beyond date of donation. Of those donors who were prescribed an NSAID, we assessed how many underwent post-prescription laboratory testing for kidney function and potassium within 14 days.

Results: Of 759 living kidney donors in the study cohort, 273 (36%) had at least one NSAID prescription over a median follow up of 7.2 years (IQR 3.5-11.5). Donors with at least one NSAID prescription were more likely to be from lower socio-economic status, have an earlier donation date, have higher pre-donation eGFR, and have co-morbid gout and osteoarthritis at the index date. The proportion of donors with at least one prescription in follow-up remained stable over time (~10% per year, Figure 1). Family physicians accounted for 66% of all NSAID prescriptions. Of the donors with an NSAID prescription, 30% also filled at least one prescription for an opioid. Approximately, 10% of donors had measurements of serum creatinine or potassium within 14 days of the first NSAID prescription. The risk of acute kidney injury or hyperkalemia was uncommon in those that underwent laboratory testing (6% and 3% respectively).

Conclusions: Over one-third of living kidney donors are prescribed NSAIDs despite current guideline recommendations. Few donors had evidence of post-prescription laboratory testing, but adverse outcomes were uncommon in those who were tested. Further research assessing outcomes following NSAID use is recommended to better inform guidelines for living kidney donors.

ID#99

Title: Kidney transplantation outcomes among patients with multiple myeloma – case series and long term follow up

Hon Shen Png - St Joseph's Healthcare Hamilton

Background: Kidney transplantation (KT) is rarely performed for patients with multiple myeloma (MM) and end stage kidney disease due to concerns for poor kidney and overall outcomes. Little is known about the outcomes of MM patients with ESKD whoreceived KT in Canada.

Methods: We retrospectively reviewed the characteristics and outcomes of MM patients who underwent KT at our centre between 2010 to 2023. We reported the unique challenges and outcomes in our cohort of MM patients who received KT.

Results: 8 patients were included in the study. All patients were staged as International Staging System III. Five were in complete remission (CR) before KT, 2 were in very good partial remission (VGPR), and 1 had MM relapse after autologous stem cell therapy (ASCT) requiring lenalidomide/dexamethasone and achieved VGPR prior to KT. Median waiting time to KT after ASCT was 42 months (range 28-64 months); 2 patients had solid organ tumors requiring treatment before KT. Maintenance therapy was present for 3 patients at time of KT (each received ixazomib, dexamethasone and thalidomide respectively). During median follow up of 41 months (range 14 to 127 months), 3 patients developed biopsy proven acute rejection at 2, 8 and 25 months respectively. Four (50%) patients had MM relapse at 6, 8, 17 and 26 months respectively. There were 2 graft losses, both were secondary to MM relapses.Death-censored graft survival at 1, 3 and 5 years after KT were 100%, 83%, and 83% respectively. Overall survival at 1, 3 and 5 years after KT were 100%, 67% and 50% respectively. Three of four patients with MM relapse died of infectious causes.

Conclusion: Early MM relapse after KT is common. Compared to patients who achieved CR prior to KT, those who achieved VGPR had similar outcomes after KT. KT provides reasonable survival benefit to MM patients.

ID#100

Title: Kidney transplantation outcomes among patients with multiple myeloma - systematic review of case reports and case series

Hon Shen Png - St Joseph's Healthcare Hamilton

Background: Registry data do not provide sufficient information on appropriate waiting time before kidney transplantation (KT) among patients with multiple myeloma (MM) after autologous stem cell transplantation (ASCT), acceptable MM treatment response prior to KT, and the outcomes after KT.

Methods: Comprehensive search on electronic databases (MEDLINE and EMBASE) from inception to March 19, 2024 were carried out using appropriate keywords and Medical Subject Headings terms. We included case reports and case series of individuals fulfilling diagnosis of MM and received treatment with or without ASCT before KT. We also included 8 patients of our own experience into data analysis.

Results: A total of 15 articles and 63 KTs were included in the analysis. 49 patients (77.8%) had an ASCT prior to KT. Prior to KT, MM remission status of complete remission (CR), very good partial remission (VGPR), and partial remission (PR) were achieved in 37 (58.7%), 14 (22.2%) and 4 (6.3%) patients respectively. Median wait time to KT after MM treatment was 36 months. Overall survival at 1, 3 and 5 years were 96.7%, 71.0%, and 62.3% respectively. MM relapse-free survival at 1, 3, and 5 years were 75.9%, 54.1%, and 48.8% respectively. Death-censored graft survival at 1, 3 and 5 years were 93.5%, 87.8%, and 78.8% respectively. MM relapse was the main cause of death and graft loss. Rejection was reported in 16 patients (25.3%). Wait time to KT after MM treatment shorter than 24 months did not affect patient survival, graft survival, nor MM-relapse rate. MM remission status prior to KT showed a trend towards lower MM-relapse rate after KT ($p = 0.119$).

Conclusion: Outcome of MM patients receiving KT are acceptable but significant morbidity remains. Shorter wait time to KT after MM treatment is not associated with poorer outcome and may be considered.

ID#101

Title: Bacterial infection is associated with expansion of intragraft CD8+ effector memory T cells in lung transplant recipients with chronic lung allograft dysfunction

Sumiha Karunagaran - University Health Network

Background: Bacterial recolonization of the allograft is common in recipients with suppurative native lung disease (cystic fibrosis and bronchiectasis) since the host sinotracheal tract is not replaced during lung transplantation (tx). Certain bacterial proteins reach the cytosol of host cells, which can then be degraded and presented on MHC-I molecules to CD8+ T cells. Others have shown that cytotoxic CD8+ T cells contribute to chronic lung allograft dysfunction (CLAD) pathogenesis, but whether this is related to bacterial infection is unknown. Here, we assess the intragraft immune environment in CLAD lungs with and without bacterial infection.

Methods: Using a 42-marker panel, we performed time-of-flight mass cytometry (CyTOF) analysis on single-cell suspensions of CLAD (n=23; collected at time of re-tx) and non-tx (n=9; donor and lobectomy) lung tissue. Dimensionality reduction was applied on CD45+ leukocytes and cluster identification, characterization, and regression (CITRUS) was used for differential discovery. Imaging mass cytometry (IMC) was performed on 1x1mm regions of interest on sections of formalin-fixed paraffin-embedded CLAD (n=8) and non-tx (n=4) lungs.

Results: CITRUS analysis revealed CD8+ PD1+ CD27+ CD69+ CD45RO+ effector memory T cells (CD8+ EM T cells) as the most significantly different population between groups. A notable subset of these cells expressed CD103, consistent with tissue residency. Strikingly, this CD8+ EM T cell population was specifically expanded in recipients with suppurative native lung disease (p=0.0019; Fig 1) and those with significant bacterial colonization/infection at time of re-tx (p=0.0099). CD8+ EM T cells localized near macrophages and B cell follicles within lung lymphoid tissue (Fig 2).

Conclusions: The expansion of tissue-resident CD8+ EM T cells within lymphoid tissue in CLAD lungs is associated with both pre-tx and post-tx bacterial colonization/infection. Based on these findings, we propose that the tissue immune environment during chronic rejection may vary depending on native lung disease and infection status.

ID#102

Title: Virtual reality and gameplay as a model for exercise rehabilitation in pediatric solid organ transplant patients. A patient and family led initiative

Christopher Buckland - British Columbia Children's Hospital

Background: There are many health benefits for pediatric Solid Organ Transplant (SOT) patients who engage in regular physical activity. However, a major barrier to ongoing participation is a lack of interest. Recently, a patient family within the Multi-Organ Transplant Program at British Columbia Children's Hospital described their use of virtual reality (VR) gameplay for physical activity. We conducted a feasibility study to assess VR gameplay as a form of physical activity for our SOT patients.

Methods: All eligible 13-18-year-old SOT patients within our Program were approached for consent. Participants engaged in an 8-week VR exercise program followed by 8-weeks of non-gameplay. The self-directed VR exercise program consisted of three games and a weekly requirement of exercising 3x/week for 30 minutes/session (24 sessions). Heart rate (HR) during VR exercise was recorded using a smart watch. An exercise treadmill test to volitional fatigue was administered prior to the start of the VR exercise program, post-VR program and following the non-gameplay period. Parameters measured during the exercise test included HR, V̇O2peak and other respiratory exchange variables.

Results: The recruitment rate was 12/59 (20%); 5/12 participated in VR exercise. The median age of participants was 16.1 years (14.3-16.8). Four of five participants met criteria for a maximal exercise test. Peak exercise test HRs ranged from 150 to 203 bpm. Participant Z-scores for absolute V̇O2peak ranged from -2.85 to -1.38 and did not improve with VR exercise. The median number of gameplay sessions completed was 10 (8-22). The duration of gameplay sessions was 31 minutes (26-35). The percentage of time spent at > = 50% of peak HR during gameplay ranged from 85%-100%.

Conclusion: VR gameplay can elicit an effective exercise stimulus. However, regular weekly exercise in our study was low and this may have contributed to the lack of improvement in V̇O2peak with VR exercise.

ID#103

Title: Examining the unique and dynamic profile of endothelin-1 in ex vivo lung perfusion perfusate to predict clinical outcomes

Abby McCaig - University Health Network

Introduction: Lung transplantation is the primary intervention for end-stage lung diseases, yet limited donor organs are accepted for transplantation due to concerns of poor patient outcomes. Ex vivo lung perfusion (EVLP) enables advanced assessment of marginal donor lungs. Sampling perfusate circulating through EVLP can be used to measure levels of biomarkers to determine lung viability. Endothelin-1 (ET-1), a chemokine that promotes vasoconstriction, has been proposed as a biomarker for donor lung assessment, yet the temporal dynamics of ET-1 remains unknown. Our objective is to investigate the changes in endothelial function during lung transplant by evaluating the dynamic profile of ET-1 levels during EVLP and examining changes in ET-1 gene expression pre- versus post-EVLP.

Methods: Perfusate was collected for 35 cases at 15-minute intervals during EVLP and ET-1 levels were quantified by ELISA. Transcriptomic analysis was conducted on 85 paired human lung tissue samples pre- and post-EVLP. Gene set enrichment analysis (GSEA) and single gene analysis were used to analyze the changes in the endothelin-1 gene set.

Results: ET-1 shows a unique and dynamic profile during EVLP (Fig 1). ET-1 levels in donation after cardiac death (DCD) lungs over the first 90 min of EVLP for recipients with good outcomes (0.86±0.38 pg/mL) were significantly lower than those with poor outcomes (4.47±2.44 pg/mL) ($p=0.0019$), and significantly lower than lungs rejected after EVLP (3.76±2.10 pg/ml) ($p=0.021$) (Fig 2). GSEA revealed an upregulation of the ET-1 gene set following EVLP with significant enrichment of several genes including the END1 gene coding for the ET-1 protein ($p < 0 .0001$) (Fig 3).

Conclusion: Here, we are the first to show a dynamic profile of ET-1 not seen in any other biomarkers. These results will provide valuable information to clinicians about the endothelial function of donor lungs to make informed decisions regarding transplant suitability, leading to improved recipient outcomes.

ID#104

Title: Time-dependent kidney function is a risk factor for cardiovascular disease in kidney transplant recipients

Seoyoon Shin - University Health Network

Background: The relationship between kidney function and cardiovascular disease (CVD) among kidney transplant recipients is complex due to time-varying confounders and covariates such as recipient factors, donor factors, and transplant factors. Monitoring CVD and renal function in kidney transplant recipients is essential because these patients are at a high risk for cardiovascular events which can significantly impact graft function and overall patient health. Our aim was to determine the relationship between CVD and kidney function, while accounting for time-varying blood pressure.

Methods: We conducted a retrospective cohort study on 3130 kidney transplant recipients transplanted between January 1, 2000 and December 31, 2019. Kidney function was based on the CKD-EPI estimated glomerular filtration rate (eGFR). Cardiovascular disease was defined as major adverse cardiac events (MACE) and MACE excluding death. We used time-fixed, time-varying, and marginal structural Cox proportional hazards models to assess the association of time-dependent eGFR and MACE while adjusting for time-varying blood pressure and baseline recipient, donor, and transplant characteristics.

Results: During the median 4.47 years of follow-up, an incidence rate of 3.42 per 100 person-years was observed. We recorded 447 MACE and deaths. A time-fixed Cox model demonstrated that each 10 mL/min decrease in eGFR was associated with an increased risk of MACE (HR 1.11 [95%CI: 1.04, 1.18]). Stronger associations were observed using a time-varying Cox model for MACE (HR 1.20 [95%CI: 1.14, 1.26]).

Conclusion: Time-dependent eGFR is an independent risk factor for MACE and MACE excluding death in kidney transplant recipients. Future research on interventions to manage eGFR is needed to reduce the risk of CVD in these patients.

ID#105

Title: Exploring acceptability of Donate Now policy initiative in British Columbia: Focus group consultations

Reetinder Kaur - Providence Research

Background: For people considering living kidney donation, the concern that they may need to save their kidney for their child, family member, or friend who may need a kidney in the future may deter them from ultimately pursuing donation. Strategies to remove this disincentive are needed. This study aims to explore the acceptability of an advanced donation policy that would allow living kidney donors to nominate individuals for future prioritization for a deceased donor kidney transplant should they need one in the future.

Methods: Focus group consultations were conducted with living kidney donors, wait-listed transplant candidates, and general community members from racialized communities in which participants' views on the acceptability, potential benefits, limitations, and consequences were obtained. Preliminary results from South Asian general community participants are presented.

Results: Eight South Asian participants, aged 34 to 61 years were included. Four participants identified as women, 3 as men and 1 as a non-binary person. Six of the eight participants were born outside of Canada. Participants were supportive of the proposed policy and felt it could increase acceptability of living kidney donation in the South Asian community. Addressing the concern of a loved one potentially needing a transplant in the future was felt to be important and participants felt a policy addressing this disincentive may enhance comfort around living kidney donation among SA community members. Participants highlighted the need for clear education to ensure awareness of the policy and acknowledged the need for rules, but felt a more flexible policy may be more impactful.

Conclusion: A policy through which living kidney donors may nominate loved ones to receive a priority for deceased donor transplantation in the future was felt to be acceptable and potentially impactful at increasing living donation rates in the SA community.

ID#106

Title: Adapting Indigenous Wellness Liaison Roles to Kidney Transplantation: Results of a Priority-Setting Process

Simone Kennedy - Providence Research

Intro: The BRIDGE Initiative aims to improve access to kidney transplantation for Indigenous Peoples by implementing culturally safe navigation support for Indigenous patients, including transplant specific Indigenous Wellness Liaisons (IWL). This paper reports the results of a priority-setting process to design a transplant specific IWL program based on existing Indigenous navigation programs and through key stakeholder involvement.

Methods: Qualitative data on BC specific barriers to transplantation for Indigenous patients and a literature search of existing Indigenous navigator programs formed the basis of a proposed model for a transplant specific IWL role. A three-round priority-setting process was conducted with Indigenous transplant patients, kidney donors, Elders, multidisciplinary clinicians, Indigenous health experts, policymakers and funders. Through a series of idea generation, refinement, and ranking activities, IWL roles and qualifications were prioritized.

Results: While many existing Indigenous navigation roles are primarily hospital based, transplantation was felt to require a longitudinal ambulatory model of culturally safe navigation and support. Agreement was established on the preferred range and scope of the six core responsibilities: 1) patient advocacy, 2) communication, 3) coordination, 4) education, 5) emotional and psychosocial support, and 6) decision-making support (see Figure 1). The primary scope of care related to the pre-transplant evaluation period; however, post-transplant support was recommended during the index hospitalization and early post-transplant period. Lived experience as an Indigenous person was the most important qualification with secondary preference given to previous work experience in healthcare.

Conclusion: A transplant specific IWL should focus on a patient facing role in which Indigenous patients are supported through their pre-transplant evaluation through a broad range of supports including advocacy and coordination from a person with the lived experience of being Indigenous. These recommendations are guiding the implementation and evaluation of a provincial transplant IWL role through the BRIDGE Initiative in BC.

ID#107

Title: The metabolic changes of donor lungs during cold ischemic preservation and reperfusion in porcine lung transplantation

Lubiao Liang - University Health Network

Background:

Lung transplantation stands as a cornerstone in treating end-stage lung diseases, yet the process of cold storage preservation poses challenges due to ischemia reperfusion injury. Metabolomics offers a novel approach to understanding the dynamic tissue changes during cold ischemia preservation and post-transplantation reperfusion, thus informing targeted interventions. The objective of the present study was to determine the effects of donor lung preservation and reperfusion on metabolic changes in the lung grafts.

Methods:

Porcine donor lungs underwent cold ischemia preservation (CIT) at 4°C for 0, 6, and 30 hours. Additionally, donor lungs from brain death (BD) porcine underwent 12-hour CIT. Both 30-hour CIT and BD 12-hour CIT lungs underwent ex vivo lung perfusion (EVLP) for 12 hours and the left lungs were transplanted to recipients. Lung tissue from all groups were subjected to metabolomic analysis.

Results:

Time-dependent metabolic changes during CIT were observed, with decreased glucose levels and extracellular matrix markers, alongside increased sterol and steroid metabolites. Subsequent transplantation induced significant metabolic shifts, with elevated levels of glucose, pro-hydroxy-proline, allantoin, and urea in 30-hour CIT donor lungs in 30-hour CIT donor lungs. Conversely, both oxidized and reduced forms of glutathione, lactate, and putrescine, ascorbate, levels significantly decreased in 30-hour CIT donor lungs after transplantation. The BD group had very similar changes with 30h CIT group after reperfusion. Furthermore, differential responses in choline-conjugated lysophospholipids and prostaglandin biosynthesis were observed between the 30-hour CIT and BD groups.

Conclusion:

This study elucidates the metabolic changes of lung allografts during cold ischemic preservation and post-transplantation. Understanding these metabolic conditions may help improve donor lung quality and expand donor pool.

ID#108

Title: A pathway of excellence in organ donation and transplantation: A novel medical school curricular design project

Brianna Andrews - University of Saskatchewan

Background: Organ donation rates in Canada lag that of other OECD countries leading to a gap in need and supply, while patients with end organ failure die awaiting this lifesaving gift. Reasons for this are multifactorial, however physician lack of knowledge around organ donation may lead to missed opportunities. Studies have highlighted a significant lack of knowledge around organ donation and transplantation (ODT) amongst medical students.

Methods: Following Kern's curricular design steps, prior work from our group has identified topics of importance to primary care physicians and ODT specialists (needs assessment: Kern step 1 & 2). The objective of this project is to develop a curriculum on ODT throughout the four years of the medical school curriculum (Kern step 3). This 'Pathway of Excellence' will utilize the concept of curricular threads throughout the current curriculum (Kern step 4). Curricular threads are key concepts that can be connected to various courses.

Results: Using the local medical school as a model, a 4-year curriculum was proposed with the following curricular threads: 1) humanistic aspect of donation and transplant, 2) science of donation and transplant, 3) skills of donation and transplant, 4) communication skills, 5) showing empathy, incorporated into current courses (Table 1). Evaluation consists of personal reflections, multiple choice questions, objective structured clinical exam stations, ward-based evaluation, presentation skills, and completion of entrustable professional activities (Kern step 4). This curriculum will be open to students who show commitment and motivation to further explore knowledge in ODT. Successful students will receive a Certificate in ODT upon graduation.

Conclusions: We propose a novel curriculum in ODT for the medical school curriculum. This 'Pathway of Excellence' has the potential to improve knowledge in important topics. Further work is required around implementation and evaluation of the 'Pathway'.

ID#109

Title: Barriers to Familial Consent in Deceased Organ Donation Among Racialized and Indigenous Communities in Canada: A Qualitative Study

Simran Sandhu - UBC

Background: In Canada, over 3700 people are on the organ transplant list, with deceased donor transplants making the majority of transplants completed annually. Despite the increasing numbers of transplants, populations marginalized by race and ethnicity have lower rates of organ donation registration and are less likely to consent to donation. Gaining insight into barriers to providing consent is critical in developing strategies to address disparities. This study aimed to identify barriers to familial consent among members of racialized and Indigenous communities.

Methods: 48 participants were recruited through community-based organizations in British Columbia (BC) and included BC residents, aged over 19, who spoke English. 31 participants completed interviews and 17 took part in focus groups. Participants were oversampled for members of racialized and Indigenous communities. A case vignette was used to collect data with data analyzed using summative content analysis.

Results: Four overarching barriers were identified: 1) system-level; 2) community-based; 3) related to decision-making; and 4) informational. System-level barriers highlighted mistrust of Canadian healthcare institutions and professionals, perceived coercion, and the role of language in consent. Community-based barriers involved ideas around the deceased body, funeral, afterlife, and general perceptions of organ donation. Decision-making was affected by family dynamics and donor/recipient identity. Informational barriers such as age eligibility also influenced consent. Facilitators to address barriers include culturally diverse resources, increasing community knowledge, and providing language, cultural, and religious support to build trust and facilitate culturally safe and effective conversations.

Conclusion: This study highlights barriers and modifiable determinants to familial consent in deceased organ donation among members of racialized and Indigenous communities. Education and engagement initiatives must be targeted at the health system and community levels to fully address barriers to consent and reduce racial and ethnic disparities in organ transplantation.

ID#110

Title: A validation study of administrative data algorithms to identify pediatric solid organ transplant recipients

Simran Aggarwal - McMaster University

Background: Health administrative datasets could offer valuable insights into pediatric solid organ transplantation but first require validation. Currently, there are no validated algorithms utilizing health administrative databases to identify solid organ transplant patients and existing studies are single-centre, have small sample sizes and short-term follow-ups. This study aimed to validate administrative data by determining sensitivity and positive predictive value (PPV) when compared to direct transplant records from a large pediatric transplant centre (reference standard).

Methods: Data collected from a single-centre transplant database (1991-2011) was linked to administrative data at ICES. Data from the Canadian Organ Replacement Register (CORR), physician billing claims from the Ontario Health Insurance Plan (OHIP), and hospital procedural codes from the Canadian Institute for Health Information (CIHI) were compared to the data from the transplant centre database.

Results: A total of 347 kidney, 250 liver, 200 heart, and 28 lung transplants were performed. CIHI alone had the highest sensitivity and PPV in identifying all individual solid organ transplants (sensitivity 87-93% [95% CI 83-100%]; PPV 90-96% [95% CI 86-100%]), except in kidney, where a combination of 'CIHI or CORR' and 'CIHI or CORR or OHIP' had slightly higher sensitivity (98% [95% CI 97-100%] for both). 'CIHI or CORR or OHIP' also had slightly higher sensitivity than CIHI alone for a composite of all solid organ transplants, but no difference in PPV (see Figure 1).

Conclusions: This is the first study to validate health administrative data in identifying pediatric solid organ transplant recipients. CIHI codes are preferred for the detection of all solid organ transplants, except for kidney and combination transplants where they may be used in combination with CORR or OHIP to further increase sensitivity.

ID#111

Title: Ex vivo heart perfusion vs. cold storage of healthy hearts in extended preservation time: a juvenile porcine experimental model

Yasuyuki Kobayashi - The Hospital for Sick Children

Background

Donor-after-brain death hearts have been the majority in pediatric heart transplantation. A cold ischemic time> 4 hours was previously detected as a risk factor for post-transplant graft loss. We sought to evaluate the trajectories of the metabolism and cardiac function during ex vivo heart perfusion (EVHP) and compare the ones preserved with EVHP to the ones with cold storage in different extended periods.

Methods

Twenty-two healthy hearts were procured from 10-kg piglets and preserved in four groups with the combination of preservation method (EVHP/cold storage) and time (6/8 hours): 6hr-EVHP, 6hr-Cold, 8hr-EVHP, and 8hr-Cold. After the designated preservation, the heart was perfused in working mode (WM) for 2 hours, simulating the post-transplant status. Cardiac function was continuously assessed by the intraventricular balloon technique during preservation and by echocardiography and flow meter during WM. Arterial and venous blood samples were taken every 30 minutes. The overall significance of the time profile was assessed using likelihood ratio tests.

Results

The minimum pressure change rate gradually decreased during preservation with EVHP. Arterial lactate levels did not increase until 6 hours but started increasing sharply at 7 hours and kept rising until the end of preservation (Figure). Compared to the 6hr-Cold group, the 6hr-EVHP group showed a lower cardiac output (CO, 109% vs. 116% of normal) and higher arterial lactate levels (4.85 vs. 2.56 mmol/l, $P < 0.001$). Compared to the 8hr-Cold group, the 8hr-EVHP group also demonstrated a lower CO (74% vs. 104% of normal) and higher arterial lactate levels (20.0 vs. 4.07 mmol/l). The 8hr-EVHP group showed the greatest percent gain in heart weight (20.0%, P=0.028).

Conclusions

In this juvenile porcine model, the inferiority of EVHP to cold storage regarding hemodynamics and metabolism was observed in the setting of both 6 hours and 8 hours of preservation. The indications for pediatric EVHP should be carefully reviewed.

ID#112

Title: Sub-zero unfrozen storage is effective for prolonged storage of kidney grafts in an auto transplant porcine model

Francisco Calderon Novoa - University Health Network

Background

4°C storage remains the gold standard for organ preservation due to its simplicity and cost-effectiveness. However, even on ice, the organ is still subject to injury. Freezing is routinely used in cell preservation, since it renders the cells in a quiescent state. Nonetheless, extremely low temperatures and the freeze-thaw process lead to intracellular ice crystal formation and irreversible damage, limiting organ preservation. Our previous studies show that Cryostasis' sub-zero storage technology is feasible for short periods of time (5 hours). We aimed to determine the effects of sub-zero unfrozen storage when extending the storage time to the limits of clinical practice (24-48hs).

Methods

Kidney grafts were retrieved from 30kg pigs and flushed with HTK or Cryostasis® organ storage and flush solution (CrS), followed by 24 hours (n=6) or 48 hours (n=4) storage either on ice or at –0.5°C using Cryostasis® technology. Finally, grafts were auto-transplanted, and subjects were followed-up for seven days.

Results

All subjects showed delayed function consistent with prolonged cold ischemia. Creatinine, urea and potassium levels were similar between groups and storage times (ANOVA $p>0.05$). All pigs presented urinary output from day 3 onwards. Creatinine clearance was reduced at POD 2-3, improving at POD 6-7 (39.65 ml/min for –0.5°C group vs. 19.96 ml/min for the 4°C group). FeNa peaked at POD 2-3 and was minimal at POD 6-7 (0.4% in the -0.5°C group vs. 2.43% in the 4 °C SCS group, $p=0.67$). Specimen analysis revealed higher injury [1(0.5-1) vs. 2(0.5-2)] and inflammation [1(1-2) vs. 1.5(1.5-3)] in the 4 °C group ($p>0.05$).

Conclusions

Compared with 4°C SCS, sub-zero unfrozen storage of pig kidney grafts for prolonged times produced similar short-term results in terms of kidney function, with improved urinary parameters and less damage. The benefits of lowering the temperature even further are yet to be determined.

ID#113

Title: Can muscle ultrasound imaging be used to estimate muscle mass in kidney transplant candidates?

Muhammed Shahriar Zaman - Queen's University

Background: Sarcopenia is very common in kidney transplant candidates and can predict reduced long-term graft function and diminished graft survival after kidney transplant. Dual-energy x-ray absorptiometry (DXA) is one of the most common tools for measuring muscle mass. However, due to high cost, exposure to radiation, and limited access, a more feasible method is needed to monitor sarcopenia. Ultrasound of peripheral muscles can be an accessible, low-cost and low risk alternative. Our study aimed to examine if lower limb muscle ultrasound is associated with appendicular lean mass index (ALMI) from DXA in a group of kidney transplant candidates.

Methods: A cross-sectional study was conducted in individuals 18 years or older who were listed for kidney transplant. We measured ALMI (kg/m2) by DXA. B-mode ultrasound was used to assess muscle layer thickness of quadriceps muscles: Rectus Femoris (RF), Vastus Intermedius (VI), Vastus lateralis (VL), and cross-sectional area (CSA) of RF and Tibialis Anterior (TA) of the dominant leg. A multiple linear regression model was used to predict ALMI from ultrasound: Model 1- quadriceps muscle thickness (RF, VL, and VI), and Model 2- cross-sectional area (RF and TA). These models were developed in a cohort of lung transplant candidates.

Results: The sample consisted of 15 kidney transplant candidates (7 women); age ranged from 37 - 52 years with mean BMI of 25.2±4.2 kg/m2. The regression models were not robust to predict muscle mass from DXA with $F(3, 11) = 5.437$, $P = 0.036$, $R = 0.543$, Adjusted $R2 = 0.241$ for the muscle thickness model, and $F(2, 12) = 5.408$, $P = 0.037$, $R = 0.542$, Adjusted $R2 = 0.239$ for the muscle CSA model.

Conclusion: Muscle thickness and cross-sectional area from ultrasound showed moderate correlation but the model could not explain sufficient variability. A validation study with a larger sample is warranted.

ID#114

Title: Ex vivo delivery of autologous regulatory T cells during normothermic machine perfusion in porcine kidney transplantation

Francisco Calderon Novoa - University Health Network

Background

Normothermic ex-vivo kidney machine perfusion (NEVKP) is a novel preservation technique with the potential to assess, repair, and even modify kidney grafts. As clinical knowledge and technological advances become more readily available, NEVKP has become a platform through which different treatments may be administered. Cell therapy is a promising strategy that aims to mitigate the damage brought upon the graft by the immune response to ischemia-reperfusion. We hypothesized that administration of autologous regulatory T cells (Tregs) during organ perfusion could suppress the immune response after transplantation. We investigated the feasibility of administration of Tregs in a porcine kidney auto transplantation.

Methods

Porcine kidneys were subject to 60 minutes of warm ischemia (WI) followed by 5 hours of NEVKP. Grafts were divided into two groups: NEVKP group (n=5) and NEVKP+Treg group (n=5) in which Tregs were additionally administered during NEVKP. Porcine Tregs were isolated from peripheral blood of the same pig 4 weeks prior to transplantation and expanded in-vitro. After NEVKP, contralateral nephrectomy was performed, and grafts were auto transplanted. The subjects were followed for 3 days.

Results

All animals (n=5 in each group) survived the follow-up period. Porcine Tregs entered the renal parenchyma and retained their suppressive function. The expanded Tregs did not adversely affect either NEVKP hemodynamic parameters or post-transplant graft function. CD4-positive T-cell population in the graft was significantly lower in the Treg group (NEVKP; 39%, NEVKP+Treg; 31%, mean, $P < 0$ .05).

Conclusions

Treg administration during NEVKP prior to transplantation can suppress the immune response within the graft.

ID#115

Title: Determining mechanisms of Steen-related cell injury in a cell culture model

Kate Rokoss - University Health Network

Background: Ex-vivo lung perfusion (EVLP) is a technology that has greatly advanced donor lung assessment. EVLP may be further improved for the application of advanced interventions by supplementing therapeutic components to the EVLP perfusate – Steen solution. The effects of Steen on basic cellular functions must first therefore be established.

Methods: Cell culture models were performed to investigate the basic cellular functions and mechanisms of Steen-related cell injury. Bronchial epithelial cells (BEAS-2B) and human pulmonary microvascular endothelial cells (HPMEC) were cultured to sub-confluence and incubated at 37℃ in Steen or culture media (M199 or DMEM) for varying lengths of time (2-48h).

Results: Cell viability was significantly reduced at 2h, 4h, and 24h ($P < 0.001$) in Steen compared to culture media in both cell lines. After both 4h and 24h, ATP production was significantly reduced ($P < 0.001$) in Steen compared to DMEM in BEAS-2B. A trend towards reduced glutathione and total glutathione levels was observed in both cell lines, with significantly reduced levels in BEAS-2B cells incubated in Steen solution compared to DMEM after 24h ($P=0.007$). Glutathione peroxidase 4 (GPX4) activity was significantly reduced in Steen compared to M199 after 48h in HPMEC ($P=0.001$).

Discussion: Compared to culture media, these results suggest Steen solution induces a rapid and sustained impairment in basic cellular functions. Depletion in glutathione levels and GPX4 activity suggest underlying mechanisms related to ferroptosis – a glutathione-dependent form of ischemia reperfusion injury (IRI)-induced cell death. Further investigation into ferroptosis may provide insight into supplemental agents for the development of an improved perfusate to target IRI-induced cell death and improve the quality of donor lungs during EVLP.

ID#116

Title: Gender and regional inequities in oral and poster presentations at an international transplant congress

Kathleen Gaudio - McGill University

Background

There are gender and regional disparities in academia as women and authors from low- and middle-income countries are underrepresented in scientific publications. How they intersect is not well characterized given the selective and conventional nature of articles accepted for publication in scientific journals. Examining conference abstract presentations may inform this line of inquiry. Thus, we aimed to characterize gender disparities by country income level in abstract presentations at the 2022 annual congress of The Transplantation Society.

Methods

We included all accepted oral and poster presentations published in the Transplantation journal in 2022. We extracted the first and last names of the first and last authors and their country based on their affiliations. The 2022 World Bank classification was used to characterize country income level. Gender was predicted using Genderize.io and only those where the gender was predicted with >95% probability were included in the analysis.

Results

In 2022, there were 735 oral sessions and 420 posters. For 16 abstracts there was only one named author. Majority (92%) of abstracts originated from high-income or upper-middle income countries (Figure 1). The gender of 2002 individuals were predicted with >95% probability and were included in the analysis. Overall, 36% women were listed as first or last authors; however, 43% of the first authors were women while only 29% of the last authors were women. Also, while the proportion of women first and last authors was higher among higher-income countries, they lagged behind the proportion of men first and last authors (Table 1).

Conclusion

There are inequities in knowledge dissemination at the academic congress and gender disparities are noted across all income levels to varying extent. A better understanding of factors contributing to this observation may help advance equity in academic transplantation and progress and strengthen the field of transplantation globally.

ID#117

Title: Travel burden in kidney transplant patients in Canada, 2018-2022.

Katrina Sullivan - Canadian Institute for Health Information

Background:

With transplant centres mostly concentrated in large urban areas, patients across Canada may experience high geographic and systemic barriers to accessing these complex, life-saving procedures. Our study aimed to quantify these barriers through a measure of travel burden.

Methods:

Patients who received a kidney transplant (including combination) in Canada (excluding Quebec) between April 2018 and December 2022 were identified in CIHI's Canadian Organ Replacement Register. Using this cohort as the reference, additional geographic variables and fields from CIHI's Discharge Abstract Database were used to assess five aspects of travel burden: distance travelled, likelihood of accompaniment, road network availability, whether care was scheduled, and whether care was provided close to home. Travel burden was measured on a 5-point ordinal scale that ranged from "very low" to "very high", based on outcomes of conditional logic.

Results:

There was considerable provincial and territorial variation in the degree of travel burden faced by kidney transplant recipients (Figure 1). Kidney transplant patients from provinces with no transplant programs faced the highest degree of travel burden, with 100% of patients categorized as having "very high" burden in Northwest Territories, Nunavut, and Newfoundland. Over 90% and 80% of New Brunswick and Prince Edward Island patients, respectively, experienced "high" or "very high" travel burden. Even kidney transplant recipients living in provinces with at least one transplant centre experienced variable travel burden. For example, while most patients in Alberta, Manitoba, and Ontario experienced "very low" or "low" travel burden, burden was more broadly distributed across the 5-point scale in British Columbia, Saskatchewan, and Nova Scotia (Figure 2).

Conclusion:

Despite kidneys being the most commonly transplanted organ, travel burden is experienced by many Canadians trying to access this critical procedure. This analysis may inform equity in access conversations, as well as inform discharge planning in the health system.

ID#118

Title: Unbiased proteomics analysis distinguishes chronic and acute antibody-mediated rejection in DSA+ kidney transplant recipients

Kieran Manion - University Health Network

Background: Nearly 50,000 Canadians have end-stage renal disease, for which transplantation with a new kidney is the best treatment; however, over 50% of grafts fail by 10 years. This is due mainly to antibody-mediated rejection (ABMR), where recipient donor-specific antibodies (DSA) can drive tissue injury. Unfortunately, presence of DSA alone is not sufficient to predict ABMR, as up to 60% of DSA+ patients do not develop rejection. We aim to identify factors regulating kidney protein expression in DSA+ kidney transplant recipients with and without ABMR.

Methods: Kidney biopsies were obtained from DSA+ kidney transplant recipients (Table 1) with no rejection (NR; n=45) or ABMR (acute, n=25; chronic, n=25; mixed ABMR/cellular rejection, n=25). Glomeruli (glom) and tubulointerstitium (TI) extracted from kidney biopsies using laser capture microdissection were digested to peptides and analyzed by liquid chromatography mass spectrometry. MaxQuant and Perseus software were used for protein identification and differential expression. Differentially expressed proteins (ANOVA, $p < 0.05$) were mapped to signalling pathways using the pathDIP database (FDR-BH, $q < 0.05$).

Results: 180 glomerular and 325 tubulointerstitial proteins were significantly differentially expressed between DSA+ patients with NR or with a subtype of ABMR (Fig1). Proteins upregulated in acute or mixed ABMR mapped significantly to pathways for MHC and interferon (IFN) signalling in TI (MHC pathway, q=5.5e-12; IFN signalling, q=3.3e-8). In contrast, proteins upregulated in chronic ABMR mapped to the complement cascade (glom, q=2.9e-3; TI, q=6.8e-11) and extracellular matrix organization (glom, q=2.1e-7; TI, q=2.5e-4) in both compartments. DSA+ patients with any ABMR subtype showed significant downregulation of proteins linked to pyruvate metabolism (glom, q=2.7e-4; TI, q=6.9e-14) in both compartments compared to NR (Fig2).

Conclusion: Our results suggest that while both acute and chronic ABMR in DSA+ kidney transplant patients involve altered metabolism, distinct immune-mediated mechanisms may drive tissue damage in the individual subtypes.

ID#119

Title: The impact of thoraco-abdominal normothermic regional perfusion on lung grafts evaluated by ex-vivo lung perfusion

Matthieu Glorion - CHUM

Background :

Thoraco-abdominal normothermic regional perfusion (TA-NRP) is a novel strategy for harvesting hearts from donors after cardiocirculatory death (DCD). Its impact on lung grafts, compared to the current standard of direct procurement (DP), remains unclear.

Methods :

A DCD porcine model was utilized. After 30 minutes of functional warm ischemia, two groups were compared: the TA-NRP group (n=4) underwent 60 minutes of in-situ reperfusion with extracorporeal circulation, while the DP group (n=4) did not. Subsequently, lungs from both groups underwent perfusion with EVLP (Lund protocol) for 4 hours to assess function and transplantability.

Results :

Both groups' lungs were deemed suitable for transplantation. Parameters such as exchange capacity (PaO2/FiO2), lactate, and glucose levels in the perfusate showed no significant differences between the groups (549±68 vs. 551±64 mmol/L, p=0.69), (8.2±2.7 vs. 7.8±2.9 mmol/L, p=0.89), and (8.7±2.0 vs. 8.0±0.5 mmol/L, p=0.69) respectively. However, lung weight gain (TA-NRP: 7.2±5.9 vs. DP: -2.0±4.2%, p=0.03) and pulmonary vascular resistance (p=0.04) were higher in the TA-NRP group, while static pulmonary compliance (p=0.049) was lower.

Conclusion :

TA-NRP does not significantly affect the transplantability of lung grafts in a DCD porcine model. This method appears safe for expanding the pool of organ donors in the context of DCD.

ID#120

Title: The impact of donor-recipient size mismatch measures on post-transplant outcomes in adult kidney transplant recipients

Christie Rampersad - University of Toronto

BACKGROUND: The impact of donor-recipient body size mismatch as surrogates of nephron endowment and metabolic requirements is not well established. We sought to evaluate the association of size mismatch measures and post-transplant outcomes.

METHODS: This single-centre study evaluated adult donor-recipient kidney transplant pairs from 2000 to 2022 at the University Health Network. Size mismatch at transplantation was classified as difference in weight (kilograms), body mass index (BMI, kg/m2), and body surface area (BSA, m2) and divided into quartiles with very low and low quartiles denoting favourable mismatch (i.e., relatively larger recipient and smaller donor), and high and very high quartiles denoting unfavourable mismatch (i.e., relatively smaller recipient and larger donor). Multivariable Cox proportional hazards models were used to assess associations of size mismatch and death-censored graft failure (DCGF), all-cause graft failure (ACGF), and death with graft function (DWGF). Multivariable linear regression models assessed estimated glomerular filtration rate (eGFR) at 1-year post-transplant across size mismatch quartiles.

RESULTS: There were 3015 donor-recipient pairs with 22491 person-years follow-up to DCGF. Compared to a reference group with low mismatch, very high mismatch in weight (HR 1.45 [95% CI: 1.04, 2.04]) and BMI (HR 1.64 [95% CI: 1.18, 2.27]) were associated with significantly increased risk of DCGF. Very high mismatch was also associated with increased ACGF across all size measures, and with DWGF when assessed by BSA difference (Table 1). High and very high mismatch were associated with stepwise lower 1-year eGFR with all size measures, while eGFR was higher in recipients with very low weight or BSA mismatch (Table 2).

CONCLUSION: Our study showed significantly increased risk of graft failure for donor-recipient pairings with very high unfavourable size mismatch. Associations between size mismatch and 1-year eGFR corroborate these findings mechanistically. Future studies should explore impacts of optimizing size matching on post-transplant outcomes.

ID#121

Title: ABO-incompatible heart transplantation following enzymatic A-antigen removal in a mouse model: A-antigen re-expression and prevention of early antibody-mediated rejection

Tate Erickson - University of Alberta

Background: The ABO histo-blood group barrier challenges equitable organ allocation due to risk of rapid antibody-mediated rejection (AMR) of ABO-incompatible transplants (ABOi-Tx). Allocating rare organs is particularly challenging in pediatrics, where donor size is also an important consideration. We showed 20+ years ago that ABOi heart transplantation is safe in infants but progress is still needed for older children. Enzymatic reduction of ABO-A-antigen using Azymes (FpGalNAc deacetylase and FpGalactosaminidase) has converted human ABO-A organs to ABO-O. However, the effectiveness of Azymes in preventing early AMR remains unclear. A-transgenic (A-Tg) mice constitutively express A-antigen on vascular endothelium and can be used to model ABOi-Tx. We used this model to evaluate A-antigen re-expression kinetics after Azyme treatment and determine whether early AMR is prevented by pre-transplant donor Azyme treatment.

Methods: Following iv administration of Azyme (or control), hearts from A-Tg C57BL/6 mice (male/female, n=4/4; 15-19 weeks old) were heterotopically Tx into sex-matched wild-type C57BL/6 recipients and harvested 1-7d later. To model AMR, wild-type recipients were Tx with A-Tg hearts (+/- Azyme treatment) then administered mouse anti-A antibody and rabbit complement. Graft function was assessed by palpation 1d post-Tx; A- and H-antigen expression and C4d deposition were assessed by immunohistochemistry.

Results: Azyme-treated A-Tg grafts had minimal A-antigen staining and were H-antigen positive 1d post-Tx (Figure-1), showed weak A-antigen staining 4d post-Tx, and resembled untreated grafts 7d post-Tx. In the AMR model, untreated grafts showed C4d deposition (Figure-2), morphological features consistent with AMR (Table-1), and reduced graft function, whereas Azyme-treated grafts did not.

Conclusion: Cardiac graft A-antigen re-expression following Azyme treatment occurred within 7d post-Tx. Preliminary studies showed that A-antigen removal by Azyme treatment prevented early AMR. Clinical application of Azymes may permit ABOi Tx, utilizing organs otherwise disrcarded and offering lifesaving treatment to children for whom compatible organs may not be found.

ID#122

Title: Expression of TRAIL and TRAIL receptors in airway epithelial cells in chronic lung allograft dysfunction

David Sebben - UHN

Background: Chronic lung allograft dysfunction (CLAD) remains the main cause of death after lung transplantation. Club cells, an airway epithelial subtype with anti-inflammatory properties, are defined by club cell secretory protein expression and are depleted in CLAD. Mechanisms underlying club cell loss in CLAD are unclear. We have observed increased TUNEL staining, suggesting increased apoptosis, and increased gene expression of tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) and TRAIL-receptor-1 (TRAIL-R1) in club cells in CLAD lung explants. Here, we evaluated expression of TRAIL and TRAIL receptors at the mRNA and protein levels in epithelial cells from bronchoscopic small airway brushings of CLAD, acute lung allograft dysfunction (ALAD), and stable patients.

Methods: Brushings obtained post-transplant (4 stable, 2 CLAD, 2 ALAD) underwent single-cell RNA-sequencing (scRNAseq). Extrinsic apoptosis-related transcripts were assessed. Flow cytometric analysis was conducted separately (10 stable, 3 CLAD, 5 ALAD) to measure active caspase-3 and surface TRAIL protein on epithelial cells.

Results: ScRNAseq analysis showed an increased extrinsic apoptosis gene module score, driven by TRAIL, in club cells (Cluster 3), compared to other epithelial clusters (Fig.1A). A significant increase in TRAIL and trends towards increased TRAIL-R1 and TRAIL-R2 gene expression was observed in club cells of CLAD/ALAD compared to stable patients (Fig.1B). At the protein level, club cells expressed caspase-3 and TRAIL similarly in CLAD/ALAD and stable patients (Fig.1C). There was a trend towards higher caspase-3 expression in non-club epithelial cells in CLAD (Fig.1C).

Conclusion: Data suggests increased TRAIL gene expression in club cells in CLAD/ALAD. While this may cause widespread epithelial death, upregulation of TRAIL-R1/R2 in club cells suggests increased susceptibility to TRAIL-mediated apoptosis. Future studies will investigate protein expression of TRAIL receptors and differential epithelial responses to soluble TRAIL. This work will provide insight into a potential mechanism driving club cell loss in CLAD.

ID#123

Title: The Impact of High Intensity Training and Sports on Individuals Post Solid Organ Transplantation: A Narrative Review

Tania Janaudis-Ferreira - McGill University

Objectives: High intensity exercise in individuals post solid organ transplant (SOT) remains a largely understudied phenomenon encompassing potential benefits, risks, and yet vague optimal training protocols. This narrative review aimed to explore the impact of high-intensity exercise protocols and strenuous sports on solid organ transplant recipients (SOTRs).

Methods: We conducted a narrative review of intervention studies encompassing any design that included high-intensity exercise training post SOT, and cross-sectional or case studies of strenuous sports, and activities performed by SOTRs. We used MEDLINE to search for relevant articles. Subsequently, a manual search for additional articles was completed and the results were summarized.

Results: The search from MEDLINE produced 100 articles with no duplicates, and 37 full text articles were reviewed for eligibility in which 16 met the criteria. A total of 34 articles were included, with 18 identified through additional manual searches. Overall, 17 high intensity, 6 strenuous sports and activities and 9 case studies were retrieved. High intensity and strenuous exercise appears to be safe among stable SOTRs. High intensity protocols consistently demonstrated improvement in VO2peak, and reduction in coronary artery disease prevalence with inconsistent findings in body composition, health related quality of life outcomes, and cardiovascular biomarkers. It induced similar or greater effects to moderate intensity exercise, however, follow-up studies indicated low retention. Pre-transplant athletes showcase notable achievements and physiological adaptations post-transplantation, highlighting the capacity for athletic performance among this population.

Conclusions: As evidenced by current literature, high intensity exercise emerges as a promising exercise method for safely improving various physiological parameters and reducing the prevalence of coronary heart disease in SOTRs. However, caution is warranted in interpreting the findings from these studies due to limitations in generalizability and other methodological limitations.

ID#124

Title: Impact of Intravenous Levothyroxine Administration in Donor Heart Offers and Utilization Rates

Aditi Venkatraman - University of Toronto

BACKGROUND:

Hemodynamic instability and abnormal cardiac function are major factors contributing to non-utilization of donor hearts. Observational data suggests levothyroxine administration can reverse donor hemodynamic instability and improve left ventricular ejection fraction (LVEF). Thus, intravenous levothyroxine (LT4 IV) has been selectively used in donor care. We assessed whether standardized LT4 IV administration in donor hearts with reduced systolic function impacted donor utilization.

METHODS:

We conducted a sub-analysis of our donor QI registry, which included all prospective donor heart offers from August 2023-April 2024 with LVEF of less than 50%. We assessed LT4 IV dose at the time of offer. Standardized LT4 IV administration was defined as 100 mcg followed by 50 mcg every 12 hours. Donor demographics, clinical data, and utilization outcomes were collected and managed using REDCap.

RESULTS:

Of 28 donor heart offers with LVEF 4 hours.

CONCLUSION:

LT4 administration was associated with a non-statistically significant increase in donor heart utilization. A larger sample size is required to evaluate the true impact of LT4 on donor utilization.

ID#125

Title: Consensus Conference to Define a High-Quality Living Kidney Donor Evaluation

Seychelle Yohanna - McMaster University

Background: A key barrier to patients receiving a living donor kidney transplant is a lengthy and burdensome donor evaluation process Across Canada, living donor programs are working to improve the donor evaluation process, but there is no guidance on the elements of a high-quality evaluation or on how to measure their performance.

Methods: In collaboration with Canadian Blood Services, we will host a national consensus conference to define what a high-quality living kidney donor evaluation entails, to determine metrics for a high-quality living donor evaluation (e.g., how long it should take for living kidney donor candidates to learn if they are eligible to donate) and to establish benchmarks for these metrics. A national steering committee was formed by inviting patients, nephrologists, living donor coordinators, and staff working in provincial kidney and transplant agencies. Working groups were created to understand living donor program processes, donor evaluation data currently being collected and the patient perspective. Surveys to all living donor programs were administered to provide information needed for working groups to provide recommendations. Each working group participated in an e-Delphi to develop a set of recommendations and quality metrics.

Results: Work to date has found that living programs have variable evaluation processes, are not routinely measuring the quality of their evaluation, and patients have highlighted several important aspects of the evaluation they would like to see improved. The consensus conference will occur on September 26, 2024 and results will be presented at the Canadian Society of Transplantation Annual Scientific Meeting and published in a peer-reviewed journal.

Conclusion: By holding a pan-Canadian consensus conference, we will define what a high-quality living donor evaluation entails, including associated metrics. We anticipate this work will guide local quality improvement efforts at living donor programs and increasing access to living donor kidney transplant.

ID#126

Title: Itaconate supplementation in organ preservation solution improves donor lung function after 36 hours of hypothermic preservation in a preclinical porcine model

Gabriel Siebiger - University of Toronto

Background: Itaconate (ITA), a naturally occurring mitochondrial molecule, and its synthetic derivatives have been studied as immunoprotective metabolites in ischemia-reperfusion injury (IRI) models. Our group previously observed higher ITA expression in lungs preserved at 10ºC versus standard ice storage, and its association with better functional outcomes (Ali et al., 2021). It is unknown whether supplementing ITA, however, can improve lung transplantation outcomes.

Methods: This study explores ITA in a lung cell IRI model, selects the best ITA variant (phase 1), and evaluates adding ITA to lung preservation solution in a large animal Ex Vivo Lung Perfusion (EVLP) model (phase 2). In phase 1, human lung BEAS-2B cells were cultured to subconfluence, then exposed to cold low-potassium dextran (LPD) with or without ITA variants for 18h, followed by 48h warm reperfusion (Fig.1). Confluence and apoptosis were measured. In phase 2, porcine lungs were randomized to be flushed and preserved at 4ºC in LPD with or without dimethyl itaconate (DI; n=4 per group) for 36h, then reperfused on EVLP for 6h (Fig.2). Lung function parameters were measured, and biopsies collected.

Results: Cell culture experiments identified DI as the safest candidate, with higher confluence, lower apoptosis, and preserved morphology after 48h reperfusion compared to other ITA molecules. Porcine EVLP experiments with DI showed significantly lower airway pressures, higher lung compliance, higher oxygenation capacity, lower pulmonary vascular resistance, and lower levels of IL-8, IL-1β, IL-6, and TNF-α ($p < 0.05$) after 6h of EVLP versus controls (Fig.3).

Conclusion: We demonstrate for the first time the potential benefit of itaconate supplementation to the lung preservation solution in an extended IRI large animal model. We show DI modulates pro-inflammatory cytokine production, improving functional outcomes on EVLP, and supporting ITA's role as a key mediator of the protective effect of 10ºC lung preservation.

ID#127

Title: Combined heart-kidney transplantation in a pediatric patient: do adult criteria apply?

Brandon Noyon - CHU Sainte-Justine

Patients with chronic kidney disease (CKD) awaiting heart transplantation (HTxp) have higher posttransplant morbidity and mortality. No clear guidelines support simultaneous heart-kidney transplantation (SHKT) in children. We present the case of a complex pediatric patient with stage 4 CKD listed for a redo HTxp.

A retrospective chart review was performed. Institutional review board approval was obtained.

A 13-year-old male who had received a HTxp at age 2 for dilated cardiomyopathy (homozygous TNNI3 mutation) developed calcineurin inhibitors induced CKD. His posttransplant course was complicated by posttransplant lymphoproliferative disease, Burkitt lymphoma, and refractory posttransplant inflammatory bowel disease. Eleven years posttransplant, he developed biventricular heart failure (ejection fraction 20%) in the setting of biopsy proven acute cellular and antibody-mediated rejection (C4d positive) due to reduced immunosuppression and de novo donor specific antibodies (DSA). He was treated with a combination of steroids, rituximab, plasmapheresis, thymoglobulin and daratumumab. Kidney function worsened (creatinine clearance 28.5 ml/min/1.73m2) and he required continuous veno-venous hemofiltration to manage fluid overload. As the cardiac function did not recover, the patient was listed for a SHKT. After 4 months on the waiting list, a 29-year-old blood group identical deceased donor became available. Induction immunosuppression consisted of steroids and thymoglobulin. The heart transplant was uneventful. Four hours later, as the HTxp demonstrated normal graft function on transesophageal echocardiogram, a retroperitoneal kidney transplant was performed. Immediate good graft function was noted for both organs. No renal replacement therapy was required. Four weeks posttransplant, the patient is well with good dual graft function (ejection fraction 70%, creatinine level 67 µmol/L).

Multidisciplinary evaluation is required when considering multiorgan transplantation in pediatric patients. Sensitization from previous transplant can complicate immunological management. Adult renal function guidelines for SHKT appear applicable to children with CKD who need a HTxp, especially redo-HTxp, to reduce morbidity and mortality.

ID#128

Title: Communicating Risks to Potential Living Kidney Donors: A Systematic Review of International Literature

Sheryl Ordonez - University Health Network

Background: Although complication rates for living kidney donors (LKDs) are low, LKDs are inevitably exposed to short-term and long-term post-operative risks. There is currently limited understanding of how risks are conveyed to LKDs. To ensure that prospective LKDs make informed decisions, healthcare providers must adequately educate potential donors of risks; however, an optimal communication practice remains controversial. This systematic review evaluates published research on current practices for LKD risk communication. To our knowledge, this is the first review of its kind in the field of kidney transplantation.

Methods: A pre-defined search strategy was applied to CENTRAL, CDSR, CINAHL, EMBASE, MEDLINE, and PsycINFO databases. Studies reporting on communication, apprehension, and/or acceptance of LKD-related risks were included. The STROBE and CASP tools were used for quality appraisal.

Results: Fifty-six articles were included and qualitatively synthesized into six themes: methods of communicating risk; risk content; terminology/techniques; personalization of risk; comprehension of risk; and acceptance of risk. Risk communication methods were highly heterogenous. There appeared to be shifts from in-person to remote approaches since the pandemic and greater emphasis on multifaceted strategies (i.e. discussions with written materials). Content also varied across practices, with an emphasis on psychosocial and financial risk. Different content delivery techniques modified risk perception: participants were more likely to accept risks when phrased as “chance of survival.” Personalized risk assessments via novel prediction models offered quantitative means of tailoring risk communication.

Conclusion: Variability in the communication of risk to prospective LKD may negatively impact the patient experience and other outcomes. The quality and breadth of the literature on this topic significantly varied. Multifaceted strategies and emphasis on non-medical risk factors consider patient diversity to tailor risk communication. This review serves as an impetus for establishing more rigorous standards, while respecting the need for personalization, in communicating risk to prospective LKDs.

ID#129

Title: Towards an optimal definition of warm ischemia time in deceased donor kidney transplant

Rohit Malyala - University of British Columbia

Background:

DCD renal donors experience warm ischemic time (WIT). Long WIT with progressive hemodynamic decline is detrimental to allografts. We analyzed donor hemodynamic courses after withdrawal of life support (WLST) to determine which hemodynamic targets best defined WIT.

Methods:

142 DCD donors' post-WLST anesthesia courses were analyzed with baseline donor/recipient characteristics. The primary outcome was DGF (dialysis within one week of transplant). WIT with sequential thresholds of SBP, DBP, MAP, HR, and SpO2, from the point the threshold was met, to reperfusion time, were calculated. These threshold-based WITs were fed into a logistic regression model to predict DGF, accounting for 1) cold ischemia time, 2) recipient anastomosis time, 3) stroke as cause of death, 4) donor age, and 5) terminal creatinine. The effect sizes and p-values of each sequential threshold for WIT were plotted for each vital feature. A quality assurance study was also undertaken where formal local records for WIT and ECD status labeling were validated with the raw results from anesthesia records.

Results:

DCD recipients from 2015 to 2022 were included based on records availability. 72/142 had DGF. Baseline donor/recipient characteristics between groups were similar between recipients with and without DGF, including for ECD status (Table 1). CIs for effect sizes of sequential WIT-definitions crossed zero at MAP=70 mmHg, and HR=45. Kappa between calculated and formally documented ECD was 0.51. Average documented WIT was 21.6±11.3 min while WIT from anesthesia courses was 11.7±14.7 min (correlation coefficient 0.70).

Conclusion:

Analysis of donor agonal-period anesthesia records suggests that WIT defined starting from a MAP=70 and HR=45 is optimal. Future steps include to phenotype patterns of hemodynamic decline to ascertain other deleterious factors contributing to graft injury, and to affirm results with more data.

ID#130

Title: Initial Experience with Abdominal Normothermic Regional Perfusion, clinical and neuromonitoring outcomes

Ephraim Tang - Western University

Background: Normothermic regional perfusion (NRP) has the potential to revolutionize DCD organ procurement. However, concerns persist regarding brain perfusion, thus our group set out measure possible neurologic activity with this technique.

Methods: DCD donors over 18 years of age at our institution were eligible for inclusion. Research consent was obtained from donor families and neuromonitoring was established prior to withdrawal and continued during perfusion via EEG and TCD. Perfusion was achieved via the abdominal aorta, and IVC with supraceliac cross clamping with a venting aortotomy above the clamp. Perfusion of the abdominal organs is achieved via a portable ECMO device.

Results: Two cases have been performed at our institution thus far. A 55- and 63-year-old donor. fWIT was 18 minutes for both cases, and time from incision to perfusion was 7-8 minutes. No neurologic activity was noted in the first donor. In the second, abnormal signals were seen on EEG, and perfusion was held. This mirrored the presence of fibrillation of the heart on EKG, confirmed visually on inspection and thus perfusion was resumed. Flow and laboratory parameters were monitored (fig 1). Lactate kinetics were noted to rise at the time of transfusions, but further decline with time. Kidneys were discarded in one donor due to severe AKI. Otherwise, both liver allografts were used without evidence of reperfusion syndrome or renal dysfunction. Kidneys from the second donor were used based on urine output during perfusion. Both were noted to have immediate graft function and excellent peri-transplant outcome despite a calculated KDPI of 93%.

Conclusion: Our initial experience with A-NRP thus far confirms the absence of meaningful brain perfusion or activity. Despite the use of otherwise marginal donors, allografts were utilized with excellent outcomes. Thus A-NRP appears to be a safe modality for allograft reconditioning, without evidence of brain activity.