2019 Canadian Transplant Summit Abstract Booklet

Oct 16-19, 2019 | Banff, AB, Canada

ID: 3
Correlation Between Gene Expression and Histology in Transbronchial Lung Transplant Biopsies

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Transbronchial lung transplant biopsies (TBBx) are limited by non-specific histologic lesions and suboptimal interobserver reproducibility. Gene expression offers a potentially more precise, objective and mechanistic diagnostic approach, but it has not yet been fully utilized in lung transplants. The aim of this study was to assess the feasibility of gene expression in formalin-fixed paraffin-embedded (FFPE) lung transplant biopsies. Methods: All TBBx performed at a single institution between 01/2015 and 12/2017 were retrieved (n=43). Those without alveolar parenchyma (n=9) or residual FFPE tissue (n=2) were excluded. Concurrent mucosal biopsies (MBx) were also retrieved (n=11). Review diagnoses were assigned by a pathologist prior to acquisition of molecular data. NanoString was used to analyze a literature-derived 136-gene set, including previously-described allograft rejection and acute lung injury transcripts. Gene expression results were correlated with histology, biopsy characteristics and spirometry. Results: 30/32 TBBx and 11/11 MBx passed quality control and were included in the final analysis. TBBx were reclassified as acute cellular rejection (n=5), infection (n=5), possible antibody-mediated rejection (n=2) and normal (n=18). There were no significant differences in patient or biopsy characteristics between diagnostic groups (p>0.05). Unsupervised principal component analysis demonstrated a general correlation between gene expression patterns and histology diagnoses in TBBx (Figure 1) but not MBx. Surfactant gene expression correlated with the presence (p 0.05). Conclusion: These results suggest that, for TBBx with alveolar parenchyma, gene expression patterns generally correlate with histologic categories. Molecular analysis of FFPE TBBx can potentially be used to identify and validate molecular signatures of clinical significance, refine histologic criteria, and provide ancillary diagnostic tools.

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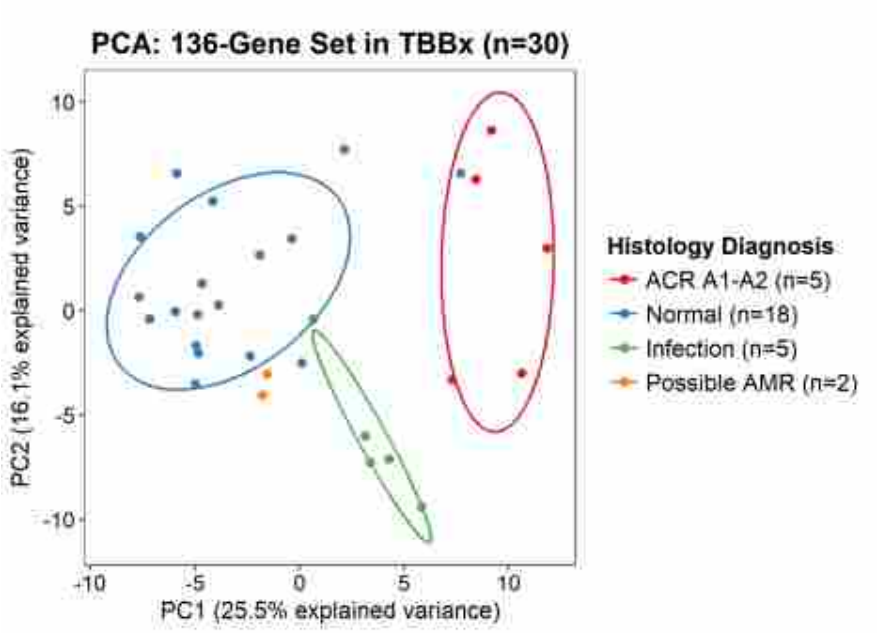

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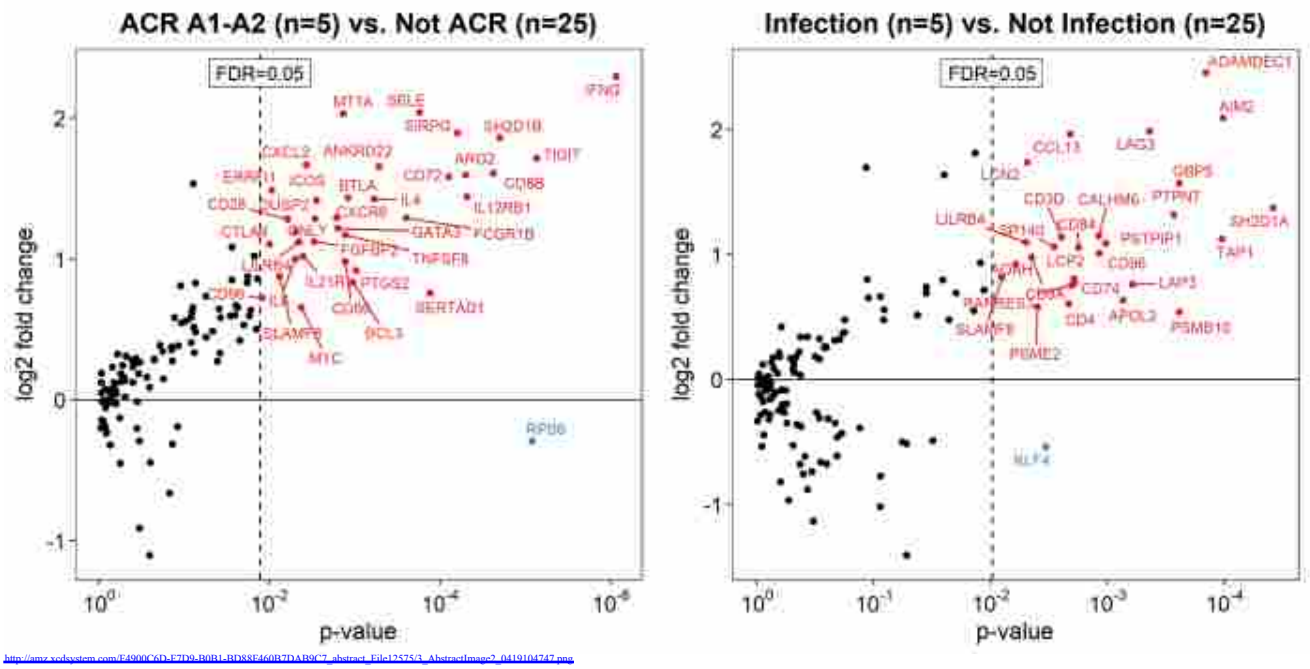

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ID: 4
Correlation Between Gene Expression and Histology in Polyomavirus Nephropathy

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

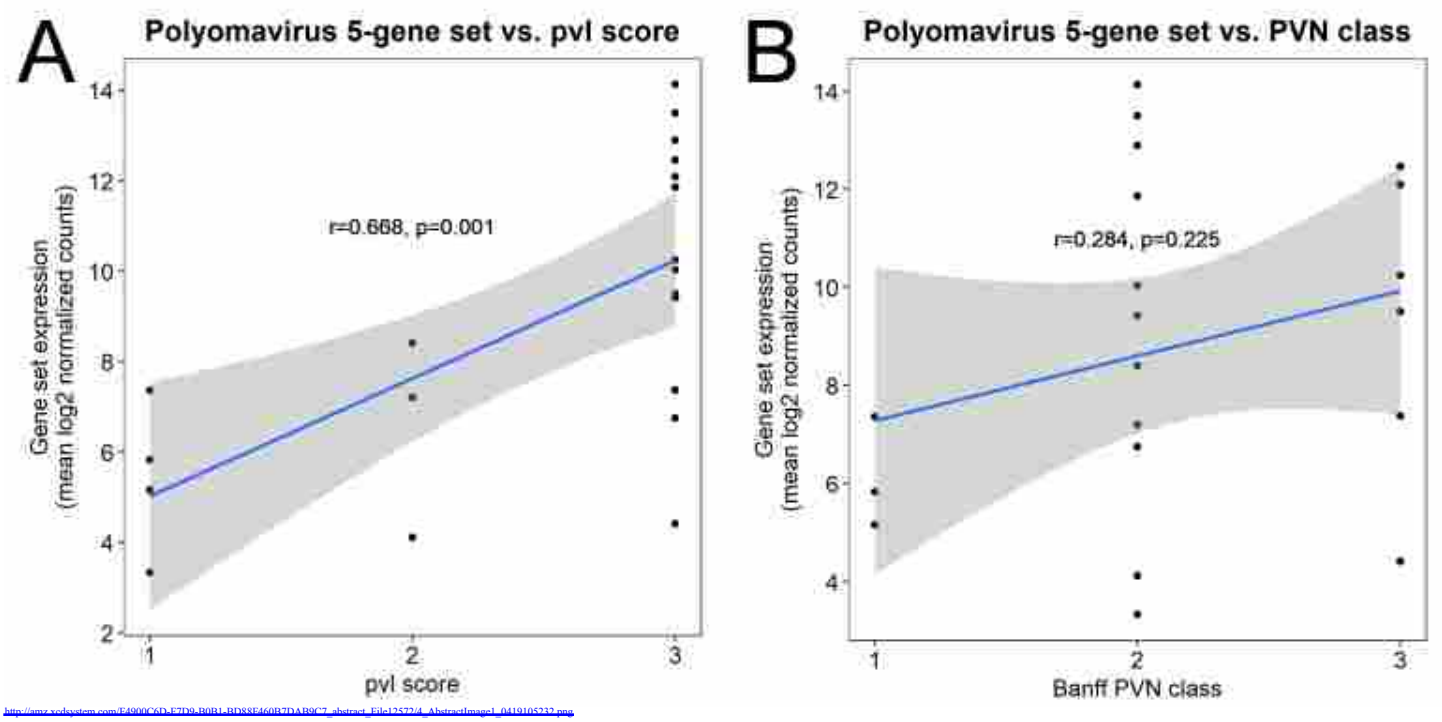
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Improved immunosuppression protocols have reduced the incidence of T-cell mediated rejection (TCMR) but still carry a significant risk of polyomavirus nephropathy (PVN). Despite requiring opposite treatments, PVN and TCMR often have overlapping clinical and histologic presentations. We previously identified a set of 5 polyomavirus (PV) genes (Agnoprotein, LTAg, VP1, VP2, VP3) with significantly increased expression in native kidney PVN vs. pure TMCR. This PV 5-gene set could potentially be used as a diagnostic adjunct for distinguishing PVN from TCMR. The goal of this study was to correlate PV 5-gene set expression with histologic and clinical features. Methods: NanoString was used to measure PV 5-gene set expression in 20 archival formalin-fixed paraffin-embedded renal allograft biopsies with histologic diagnoses of PVN. Clinical and histologic features were reviewed. Gene set expression was correlated with Banff histology lesions, PVN Class, and clinical outcome 6 months post-biopsy. Results: PV 5-gene set expression demonstrated significant correlation with pvl score (Spearmans's rank correlation coefficient = 0.668, p=0.001; Figure 1A), but not Banff PVN Class (r=0.284, p=0.225; Figure 1B) or any other Banff histology lesions (r=-0.397 to -0.031, p>0.05). Clinical outcomes 6-months post-biopsy included resolution of viremia/PVN (n=7), persistence of viremia/PVN (n=8) and development of de novo rejection (n=5); however, no statistically significant differences in PV 5-gene set expression were identified between outcome groups (p>0.05). Conclusion: These data indicate that PV gene expression correlates with pvl score (i.e. histologic burden of viral replication) but not with the recently-described Banff PVN prognostic classification system. This suggests that intragraft PV gene expression may have utility as a diagnostic adjunct, but not as a prognostic tool. Further work is warranted to assess the potential utility of endogenous (non-virus) immune-related genes in PVN.

Abstract Image 1:



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DraftModeStatus: 0

ID: 5
Molecular Characterization of Immune Checkpoint Inhibitor-Associated Renal Allograft Rejection

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

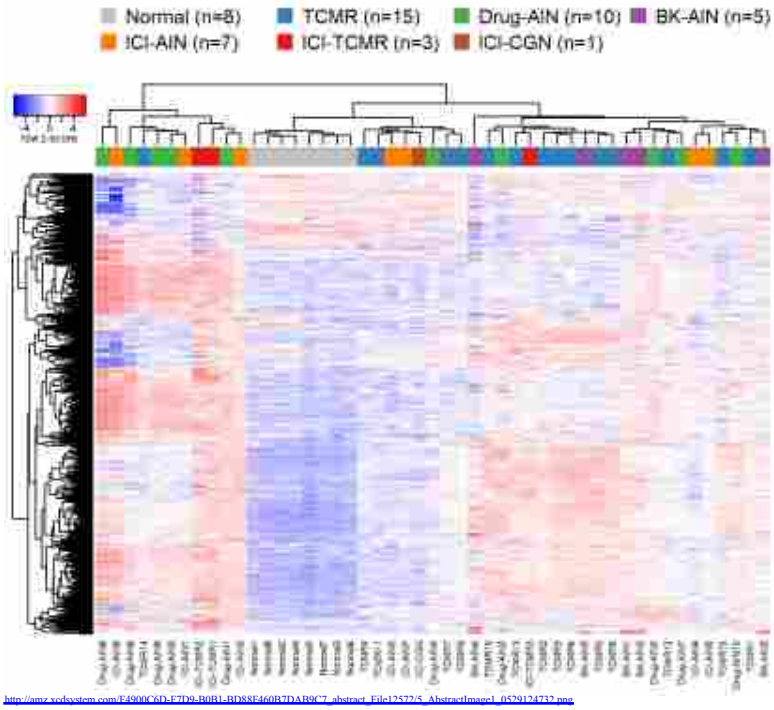
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: The use of immune checkpoint inhibitors (ICIs) for various malignancies has been associated with numerous immunological adverse events, including acute interstitial nephritis (AIN) in native kidneys and acute T-cell mediated rejection (TCMR) in transplant kidneys. The goal of this study was to further characterize these adverse events through comparative molecular analysis. Methods: NanoString was used to measure the expression of an 800-gene immune profiling panel in 49 archival kidney biopsies, including: native kidney biopsies with ICI-related AIN (ICI-AIN, n=7), ICI-related crescentic glomerulonephritis (ICI-CGN, n=1), non-ICI-related AIN (AIN, n=10) and BK virus-related AIN (BK-AIN, n=5); transplant kidney biopsies with ICI-related TCMR (ICI-TCMR, n=3) and non-ICI-related TCMR (TCMR, n=15); and normal implantation biopsies (Normal, n=8). Molecular results were then compared between groups. Results: Unsupervised exploratory analysis demonstrated significant molecular overlap between sample groups (Figure 1). No statistically significant differential gene expression was identified between ICI-AIN vs. Drug-AIN (Figure 2A) or ICI-AIN vs. ICI-TCMR (Figure 2B). However, 112 inflammatory genes exhibited higher expression and 9 genes lower expression (FDR 0.05). Similarly, no significant differences were identified between non-normal sample groups for 17 previously described antibody-mediated rejection-related genes, including 5 endothelium-associated transcripts (p>0.05). Conclusion: These results suggest that, while ICI-related AIN appears molecularly similar to non-ICI drug-related AIN, ICI-TCMR has a distinct molecular phenotype from typical TCMR. This may reflect non-specific activation of the immune system in ICI-TCMR compared with a more specific alloimmune response in TCMR.

Abstract Image 1:



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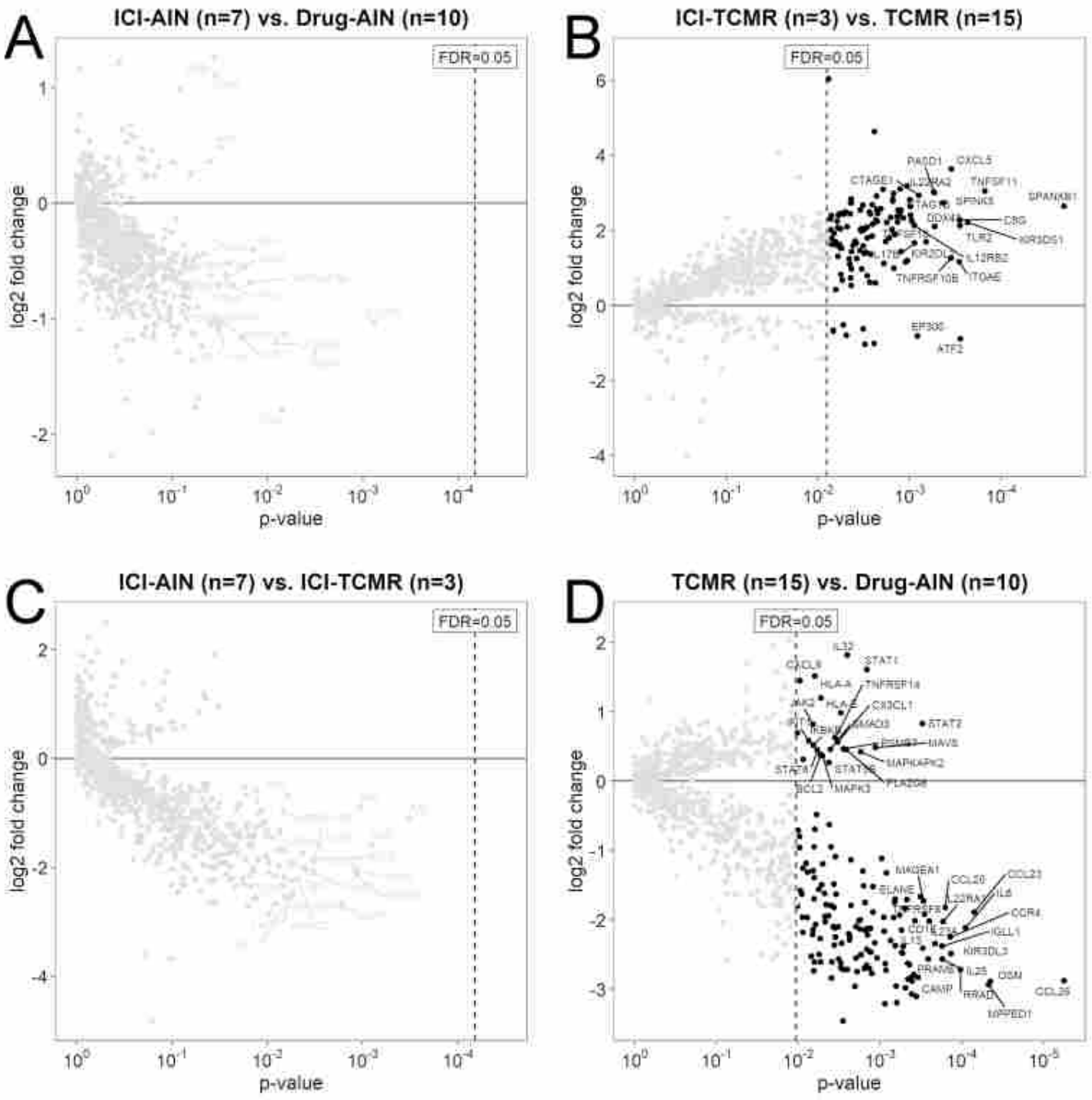

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ID: 6
Prediction of graft quality of donation after circulatory death lungs during clinical normothermic Ex-vivo lung perfusion based on a metabolomics approach

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

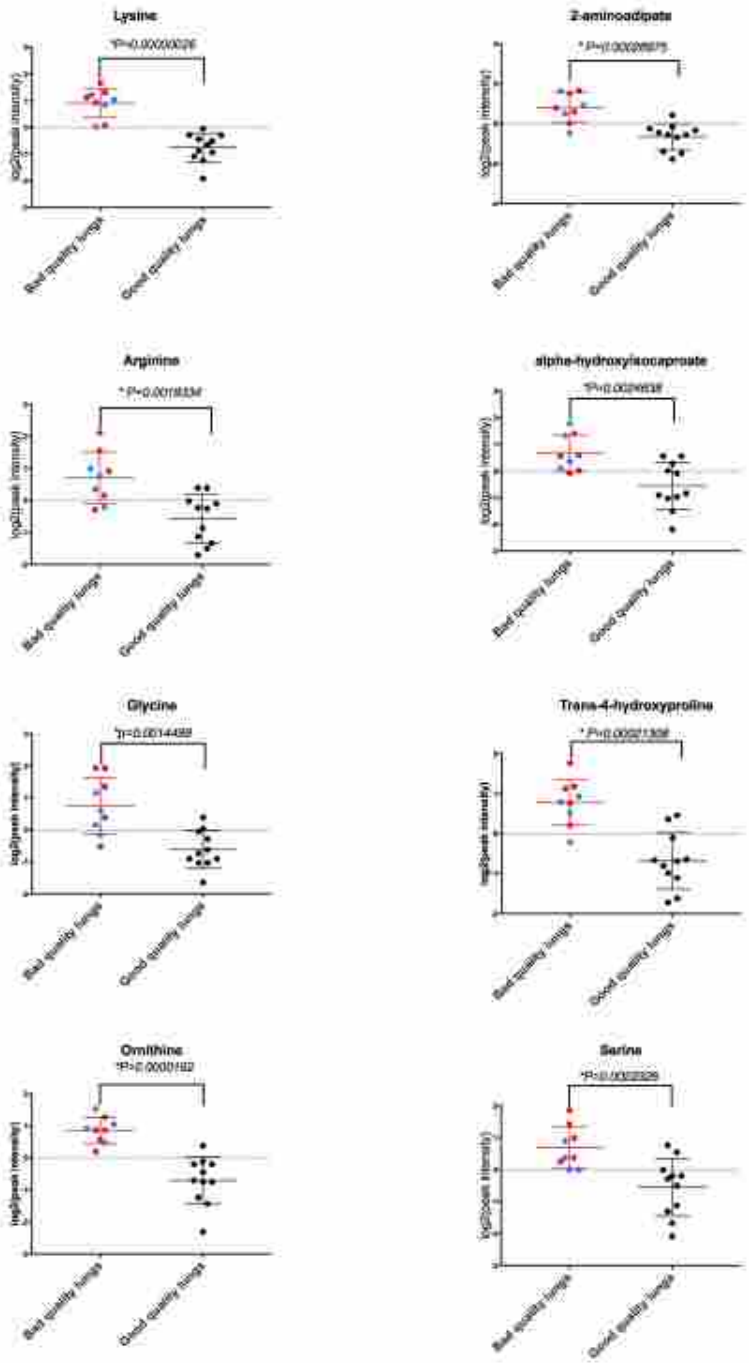
Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ex-vivo lung perfusion (EVLP) has become a widespread method to evaluate marginal donor lungs. Due to the high-risk nature of donation after circulatory death (DCD) lungs, most undergo EVLP for assessment. The difficult decision to transplant or reject a lung is guided primarily by physiological measurements, however, surgeons would greatly benefit from biochemical data to support their evaluation of lung quality. Thus, it is urgent to find specific biomarkers that meet this need, which will necessitate accurate and reliable techniques that identify biomarkers. Methods: Mass spectrometry was used to determine changes in the metabolome of 20 normothermic human DCD EVLP lungs using perfusate from the 3rd hour of EVLP in good graft quality (non-PGD3) and bad graft quality (declined and PGD3) cases. A comprehensive metabolomics data analysis was performed with Metaboanalyst 4.0 version. Results: A significant difference in concentrations of 66 metabolites were detected in bad quality lungs vs good quality lungs. Preliminary data indicate the higher release of amino acids metabolites (lysine, 2-aminoadipate, arginine, alpha-hydroxyisocaproate, glycine, trans-4-hydroxyproline, Ornithine, Serine, Alanine and 3-(4-hydroxyphenyl)lactate) in bad quality lungs as compared to good quality lungs. Conclusion: These metabolites may represent important parameters for decision making during EVLP. Furthermore, two key signaling pathways identified in this study, Aminoacyl-tRNA biosynthesis, and Glycine, serine & threonine metabolism, could be critical for lung function assessment.

Abstract Image 1:



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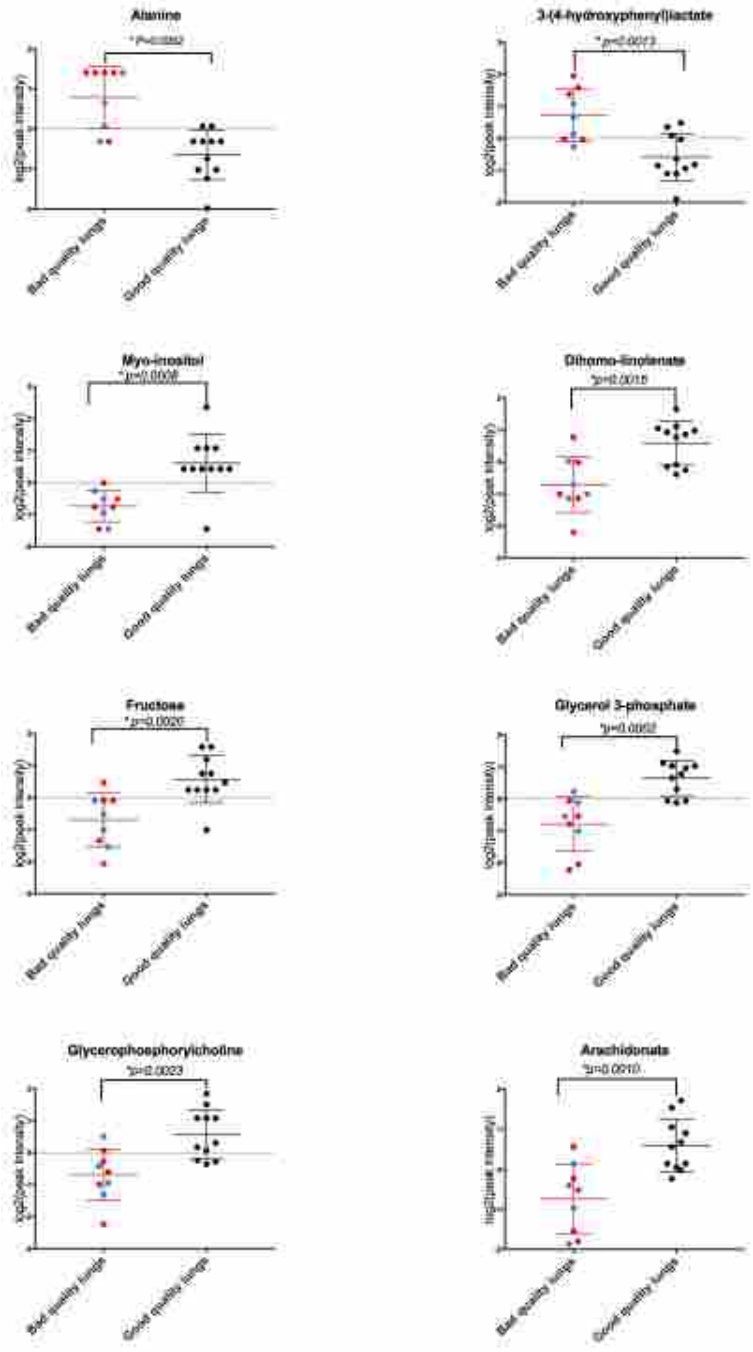

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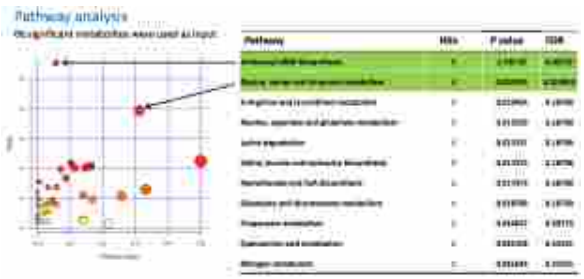

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DraftModeStatus: 0

ID: 7
Living Kidney Donation Key Success Factors for High Performing Canadian Programs

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Despite the significant advantage from living kidney donation (LKD), the rate of living kidney transplantation has declined by 11% since 2008 in Canada. It is generally accepted that key components for a high performing LKD programs exist, and when implemented, lead to improved performance. In the fall of 2018, an environmental scan was undertaken to build on previous reports and to identify key success factors of high performing living kidney donation and transplantation (LKDT) programs across Canada. The objective of this scan was to understand perspectives from both individual professional and program levels on best practices, perceived facilitators and barriers to performance, and key success factors of high performing programs in Canada. Methods: An online quantitative questionnaire was administered in February 2019 and targeted semi-structured interviews were held with LKDT program stakeholders. The e-survey questions were designed as categories representing a quantifiable practice implementation or performance influence score, using a 6-point Likert-scale. Results: 31.1 % questionnaire response rate (n=68), representing 17 LKDT sites, 3 living donation (LD) referral sites, and 10 provinces. 7 targeted stakeholder semi-structured interviews. ● There appears to be an association between implementation of best practices in living donation and better program performance. ● Examples of such practices include having a culture of transplant first, resources added to their programs to support LKDT in 2017 and 2018, and a quality assurance position to advance strategic planning at the program level. Conclusions: Canadian LKDT programs evidencing high or improved performance indicated that their performance success was most influenced by implementation of LD evaluation efficiencies, engaging program stakeholders, broadening LD identification and awareness strategies, access to quality assurance resources, increased LKDT funding, and LKDT operating room availability.

DraftModeStatus: 0

ID: 8
Apoptotic exosome-like vesicles are internalized by endothelial cells through phosphatidylserine-dependent macropinocytosis

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Member of: CDTRP

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Ischemia-reperfusion and rejection favor endothelial apoptosis, which in turn contributes to maladaptive vascular repair leading to transplant vasculopathy. Apoptotic endothelial cells (EC) release exosome-like vesicles (ApoExo) that, when uptaken by neighboring EC, shape gene expression and functions in directions conducive to endothelial dysfunction and mesenchymal transition. However, the mechanisms by which EC internalize these vesicles remain ill-defined. ApoExo were isolated by ultracentrifugation from serum-free media conditioned by primary human EC labeled with CellTracker Orange CMRA dye. Serum-starved primary human EC were then exposed to purified ApoExo in vitro. The cellular uptake of ApoExo was observed by confocal microscopy and flow cytometry using selective pharmacological inhibitors and gene knockdown. EC morphology was assessed by electronic microscopy. ApoExo displayed time and concentration-dependent uptake kinetics which were completely abolished when cells were incubated at 4°C (11.6%, P Collectively, these results suggest that ApoExo are internalized by EC through macropinocytosis. This characterization highlights potential strategies to target this internalization pathway and prevent endothelial dysfunction that contributes to transplant vasculopathy.

DraftModeStatus: 0

ID: 9
Recombinant apoptosis inhibitor of macrophage protein ameliorates transplant ischemia-reperfusion injury

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ischemia-reperfusion injury (IRI) during kidney transplantation is associated with acute rejection and long-term graft loss. During IRI, pro-inflammatory mediators (e.g. HMGB1) released from necrotic and uncleared apoptotic renal tubular epithelial cells (TECs) exacerbate tissue damage, and potentiate alloimmune injury. We uncovered that mice deficient in Kidney Injury Molecule-1 (KIM-1) were more susceptible to renal dysfunction and death after native and transplant kidney IRI than wild-type. KIM-1 is a transmembrane glycoprotein specifically upregulated on proximal TECs during renal injury, enabling apoptotic and necrotic engulfment thereby protecting against tissue damage involving local and systemic inflammation. Apoptosis Inhibitor of Macrophage Protein (AIM) is a circulating serum protein produced by macrophages and filtered by the glomerulus during IRI accumulating on necrotic debris within proximal renal tubules in both humans and mice. We further revealed that administration of intravenous recombinant AIM (rAIM) after reperfusion, facilitated native kidney recovery via KIM-1-dependent clearance of necrotic cells/debris. Here, we tested whether recombinant AIM (rAIM) can be used as a therapy that targets KIM-1 to ameliorate transplant-associated IRI in a murine model of kidney transplantation. Methods: We performed single syngeneic kidney transplants (cold ischemia time 35 mins). We evaluated serum creatinine, serum HMGB1, tubular cell death, graft inflammation and graft damage at 48 hours post-administration of rAIM (2mg/ml) or PBS (n> = 4 per group). Results: Compared to recipients treated with PBS, recipients treated with rAIM had significantly less renal dysfunction and graft damage. rAIM treated mice also showed significantly less immune cell infiltration, tubular cell death and proinflammatory cytokine production. No significant differences were found in serum HMGB1 levels between the groups. Conclusion: Our data suggests that administrating rAIM to kidney transplant recipients improve graft function by mitigating transplant-related IRI. Therefore, rAIM may be used as a therapeutic strategy to improve graft outcomes in kidney transplant patients.

DraftModeStatus: 0

ID: 10
Improving the care for pediatric transplant patients through integration of patient-reported outcome measures into clinical practice

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Member of: CDTRP

Abstract Type: Pediatric Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Subjective evaluation of medical care and treatment from the patient's perspective is increasingly important. Patient-reported outcome measures (PROMs) are defined as: "any report of the patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else". This study explores the perspectives of pediatric solid organ transplant patients, caregivers and healthcare providers on implementing PROMs into clinical practice, guided by the International Society for Quality of Life Research – User's Guide for Implementing Patient-Reported Outcomes Assessment in Clinical Practice. Methods: Semi-structured interviews were conducted with participants from five Canadian pediatric transplant centres. Maximum variation sampling was used to provide concurring and confirming data, and ensure saturation. An iterative coding process was applied with constant comparative data analysis to identify themes. Results: A total of 20 patients, 22 caregivers and 20 healthcare providers participated. Nearly all participants (95%) were supportive of implementing PROMs with the primary goals to enhance patient-provider communication – "Opens conversations"; "[Patients] state what they're feeling" and patient engagement – "Like you're part of the team". Participants discussed the potential impact of PROMs as the provision of preventative – "You'll be proactive", and holistic care – "You cannot separate medical from other aspects. [Patients] are struggling from a mental health perspective". Participants identified selected PROMs, the PedsQLTM Generic Core Scales – "Covers aspects I wouldn't usually include in my assessment" and the PedsQLTM Transplant Module – "More related to transplant patients". Recommendations included 1) assessing patients 10 years of age and older, 2) electronic administration completed remotely, prior to clinical appointments, and 3) visual data representation. Conclusion: Findings highlighted support for the implementation of PROMs into pediatric transplant practice. Future research is needed to develop implementation strategies to systematically and effectively integrate PROMs into clinical workflow and assess the impact on patient health outcomes.

DraftModeStatus: 0

ID: 11
EFFECTIVENESS OF A HOME-BASED PRE-HABILITATION PROGRAM FOR LUNG TRANSPLANT CANDIDATES: A RETROSPECTIVE CHART REVIEW

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Lung

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Rationale: In Canada, most lung transplant programs offer mandatory hospital-based pre-transplant exercise programs to optimize fitness and prevent deconditioning in lung transplant candidates. Home-based programs offer an alternative for exercise pre-transplant, giving access to rehabilitation to a larger number of patients and lower healthcare cost. Objectives: to describe changes in functional exercise capacity (6-minute walk distance-6MWD) in lung transplant candidates who participated in a home-based exercise program and determine the relationship between changes in functional exercise capacity pre-transplant and post-transplant variables. Methods: retrospective cohort study of 178 individuals who received a lung transplant between 2011-2015, participated in a home-based exercise program while waiting transplantation. 6MWD was assessed at 3 time points: time of assessment for transplant, last test prior to transplant and one-month post-transplant. Other variables included: age, sex, primary diagnosis, date of transplantation, body mass index (BMI), total hospital length of stay (LOS), intensive care unit (ICU) LOS and time on mechanical ventilation. Results: The median LOS on the waiting list was 1.8 yrs. There was a mean decrease of -27±119m between the 6MWD at the time of assessmentand the last 6MWD prior totransplantation ($p < 0 .001$; whole sample). Forty-one patients (26%) increased their 6MWD (mean change 85±113m); 72 patients (46%) decreased their 6MWD (mean -110±112m); 46 patients (29%) had no change in 6MWD (-1.5±108m). There was a weak negative correlation between change in 6MWD prior to transplant and time on mechanical ventilation ($r= -0.185$;$p < 0 .05$). When adjusted for age, gender and BMI. Change in 6MWD prior to transplant was not associated with the time on mechanical ventilation, total hospital LOS or ICU LOS. Conclusion: Most patients were able to either increase or maintain their 6MWD by participating in a home exercise program while on the waiting list. These results are similar to what has been found for hospital-based programs. Home-based exercise program may be an effective rehabilitation approach prior to transplantation.

DraftModeStatus: 0

ID: 12
Medical follow-up among living kidney donors: Adherence to a provincial protocol of follow-up after donation in a Canadian province

Member of: CST

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Medical follow-up after living kidney donation is an essential component of living donor care, yet there remains considerable variability across Canada in post-donation practices. We describe adherence to a provincial program of donor follow-up which is directed by the transplant program, but implemented by primary care physicians. Methods: We identified 338 kidney donors between 2005 and 2008 and examined their adherence to follow-up over a 7-year follow-up period. Adherence was defined as completion of either urine albumin:creatinine ratio (uACR) or serum creatinine, as captured by our provincial data system. Adherence was examined per year over the study period and the association of key donor characteristics with adherence was determined using univariate and multivariate logistics regression analyses. Results: Over 60% of all donors completed at least 1 donor follow-up test during the study period, but only 9.5% of donors completed annual testing in ALL of the 7 years. Forty percent of donors completed follow-up in the first year post-donation, and follow-up rates remained between 36.7% and 45.3% each year up to 7 years post donation (Figure). Parental and spousal donors were more adherent with follow-up, while younger and sibling donors were less adherent. Donors with lower eGFR, obesity or glucose intolerance at donation were not more likely to adhere to follow-up. Conclusion: While the majority of donors obtained at least 1 follow-up measurement of renal function within 7 years post-transplant, annual follow-up remained below 50% including among donors with higher risk characteristics. Additional resources are required to ensure more complete donor follow-up in a primary care delivered follow-up model.

Abstract Image 1:

Figure 1: The proportion of donors that completed laboratory follow-up testing in each year following donation.

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ID: 13
How do DCD donor families experience prospective clinical research participation at the time of their loved one's death in the intensive care unit?

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: For donation after circulatory-determined death (DCD), donor-management occurs in imminently dying patients after a decision to remove life sustaining therapies but before death is declared. A major challenge facing prospective clinical research in this population is the sensitive time-frame in which research consent must occur with grieving family members as decision-makers. This project is the first to investigate family members' experiences with participation in research during the process of withdrawal of life sustaining therapies in potential DCD donors Methods: We interviewed 33 family members of 28 intensive care unit patients and potential organ donors at 5 Canadian sites. Family members had consented for their dying loved one to participate in a prospective observational research study. Semi-structured interviews were conducted by phone or in person, audio-recorded, and transcribed verbatim. Results: Most participants had limited or no memory of consenting to research and of their loved one's participation. Many participants reported feeling overwhelmed and "just signing the papers" in the emotional aftermath of making decisions about withdrawal of life sustaining therapies and organ donation. When asked why they consented, several participants described either their own general support for research or described their loved one as a person who supported research as the motivation to agree to study enrollment. Participants who remembered the study affirmed that the approach for consent and processes of clinical data collection were not invasive and did not impact their experiences of end-of-life care. Conclusion: Despite being approached at an intensely challenging and emotional time, the family members we interviewed did not experience research consent or participation as a negative event. Our results confirm earlier findings about the feasibility and acceptability of prospective research in dying patients in the intensive care unit and the capacity to involve donor families as active partners in improving the donation process.

DraftModeStatus: 0

ID: 14
The Evaluation of Coronary Artery Autoregulation During Normothermic Ex Situ Heart Perfusion

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

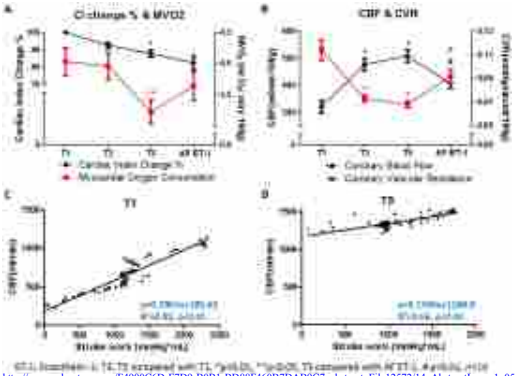
Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ex situ heart perfusion (ESHP) has emerged as a platform for reconditioning marginal donor hearts and expanding the donor pool. The coronary autoregulation is essential to maintain normal myocardial perfusion and cardiac function during ESHP. The objective is to investigate coronary autoregulation mechanism during ESHP and find ways to protect coronary function during heart preservation. Methods: The procured hearts (n=14) were perfused in ex situ working heart system at 37°C for 6 hours (with whole blood based perfusate). Coronary vascular resistance (CVR) was calculated as an indicator of coronary artery function. Hourly samples of arterial and venous perfusate from the aorta and pulmonary artery respectively, were collected for metabolic evaluation. At 1 and 5 hours of perfusion, loading of the heart will be varied by increasing or decreasing left atrial pressure to observe the corresponding response in coronary artery flow. Results: During 6 hours normothermic perfusion, cardiac function declined over time ($p<0.05$); myocardial oxygen consumption was decreased significantly ($p<0.01$). The coronary blood flow increased over time and coronary vascular resistance decreased, with a significant difference at T3 and T5 compared with T1 respectively ($p<0.01$). At T1 of perfusion, coronary artery flow shows a strong correlation with left ventricle stroke work ($p<0.01$, $R2 = 0.85$); however, at T5, the regression line is significantly different ($p<0.01$), with relative lower slope ($R2 = 0.66$), which means as myocardial function demand increases, coronary artery flow changes less than that in T1. Conclusion There is uncoupling between cardiac function and coronary artery flow. Our data reveals a poor correlation between hemodynamic stress and coronary blood flow during ESHP, indicating that the coronary autoregulation phenomenon is disturbed, which lead to excessive coronary blood flow overtime. Whether the loss of coronary artery regulation cause the decline of heart function or the mechanism of disturbed autoregulation need to be further investigated.

Abstract Image 1:



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ID: 15
Normothermic Ex-Vivo Kidney Perfusion Preservation Reliably Improves Extreme Marginal Graft Function Compared to Hypothermic Machine Perfusion

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

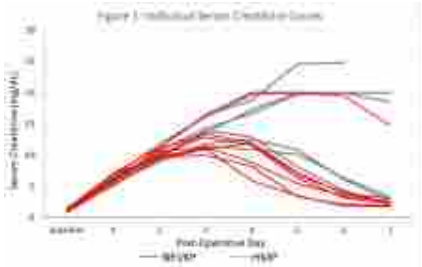
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Normothermic ex-vivo kidney perfusion (NEVKP) is an emerging technique for renal graft preservation. We investigated whether NEVKP promoted improved marginal graft function compared to anoxic hypothermic machine perfusion (HMP) in a model of donation-after-cardiac-death (DCD). Methods: Kidneys from 30kg-Yorkshire pigs were removed following 120min of warm ischemia (WI). These grafts were preserved with HMP (LifePort 1.0, n=7) or NEVKP (n=7) for 8-hrs prior to heterotopic autotransplantation. Results: During NEVKP, 120min WI grafts cleared perfusion lactate (0hr:10.48±0.93mmol/L vs 7hr:1.48±0.85mmol/L,p Conclusions: Marginal kidney grafts subjected to 120min of WI before retrieval showed reliable improvement in function following 8hrs of continuous NEVKP compared to HMP where improvement was inconsistent. This suggests NEVKP would be a preferable storage strategy for DCD procured grafts with extended WI times.

Abstract Image 1:



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DraftModeStatus: 0

ID: 16
Multiple Drug Resistant Urinary Tract Infection in Kidney Transplant Recipients: A Retrospective Cohort Study

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Abstract Objective: Urinary tract infection (UTI) is the most common infectious disease in post-kidney transplantation patients. The objective of the study was to investigate the prevalence, impact and risk factors of multiple drug resistant (MDR) UTI in kidney transplant recipients. Methods: This retrospective cohort study recruited 72 kidney transplant recipients between March 2017 and February 2018. Urine cultures performed during first 1st year of post-transplantation with reference to clinical data were also evaluated. Predesigned questionnaire was used to collect data regarding demographic, transplant related and microbiological information. Regression analysis was performed to ascertain risk factors of MDR UTI. Results: Out of 72 patients, 28 (38.9%) had culture guided clinical UTI. Overall, 59 UTI episodes were noted throughout the duration of this study. Eschericia coli were found to be the most frequent uropathogen of UTI among kidney transplant recipients (n = 32, 54.2%). MDR bacteria were responsible for 27.1% (n = 16) of the post-transplantation UTI episodes among patients, with Eschericia coli (n = 9, 56.3%) being the predominant bacterial pathogen. Most of the MDR strains of Eschericia coli (n = 7, 77.8%) were extended spectrum beta-lactamase (ESBL) positive. Female gender ($P < 0.001$), prolonged Foley's catheterization ($P = 0.002$), coexisting diabetes mellitus ($P < 0.001$) and induction of ATG therapy ($P < 0.001$) were independently associated with high risk of MDR UTI. The allograft rejection was found to be significantly higher in patients of post-transplantation UTI with MDR uropathogen ($P = 0.009$). Conclusion: In conclusion, Eschericia coli were the most prominent uropathogen of UTI with and without MDR pathogen in the present study. Female gender, prolonged Foley's catheterization, coexisting diabetes mellitus and induction of ATG therapy were the risk factors independently associated with MDR UTI in kidney transplant recipients. MDR organisms were significantly associated with allograft rejection. Keywords: Multiple Drug

DraftModeStatus: 0

ID: 17
Universal Prophylaxis with Valganciclovir versus Preemptive Therapy in Minimizing the Risk of Cytomegalovirus Infection and Disease in High and Intermediate Risk Kidney Transplant Recipients: A Single-centered Experience

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Abstract: Objective: Cytomegalovirus (CMV) is one of the most frequent viral pathogens resulting in post-transplantation infection. Universal prophylaxis and preemptive therapy has long been used to prevent and treat cytomegalovirus (CMV) infection in post-transplantation cases, respectively. The aim of this study was to compare the universal prophylaxis with valganciclovir versus preemptive therapy in minimizing the risk of CMV infection and disease in high and intermediate risk kidney transplant recipients. Methods: This single center, retrospective cohort study enrolled 63 kidney transplant recipients between March 2017 and January 2018. The outcome variables were occurrence of CMV infection and CMV disease, 1-year eGFR, allograft rejection, allograft loss and mortality within the first year post-transplantation in high risk (D+/R-) patients managed with universal prophylaxis of oral valganciclovir and intermediate risk (D+/R+ or D-/R+) patients receiving preemptive treatment. Results: Of the 63 kidney transplant recipients, 19 (30.2%) were grouped as high risk for CMV infection/disease and 44 (69.8%) were intermediate risk for CMV infection/disease. The average duration of post-transplantation follow-up was 349 (SD 136) days in the high risk cohort and 335 (SD 112) days in the intermediate risk cohort ($p = 0.56$). CMV infection was found in 15 (34.1%) of the 44 intermediate risk patients receiving preemptive therapy and in 4 (21.1%) of the 19 high risk patients receiving universal prophylaxis ($p < 0.01$). CMV disease developed in 7 (15.9%) of the 44 intermediate risk patients and in 1 (5.3%) of the 19 high risk patients ($p < 0.01$). Allograft rejection was found to be higher in intermediate risk group than in high risk group (18.2% versus 15.8%, $p = 0.44$). Allograft loss and mortality were also comparable between the intermediate and high risk cohorts (13.6% versus 10.5%, $p = 0.54$ and 0% versus 0%, $p = 0.15$, respectively). The mean eGFR at 1 year post-transplantation

DraftModeStatus: 0

ID: 18
Correlation Between Gene Expression and Cardiac Function in Ex Vivo Perfused Porcine Hearts

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

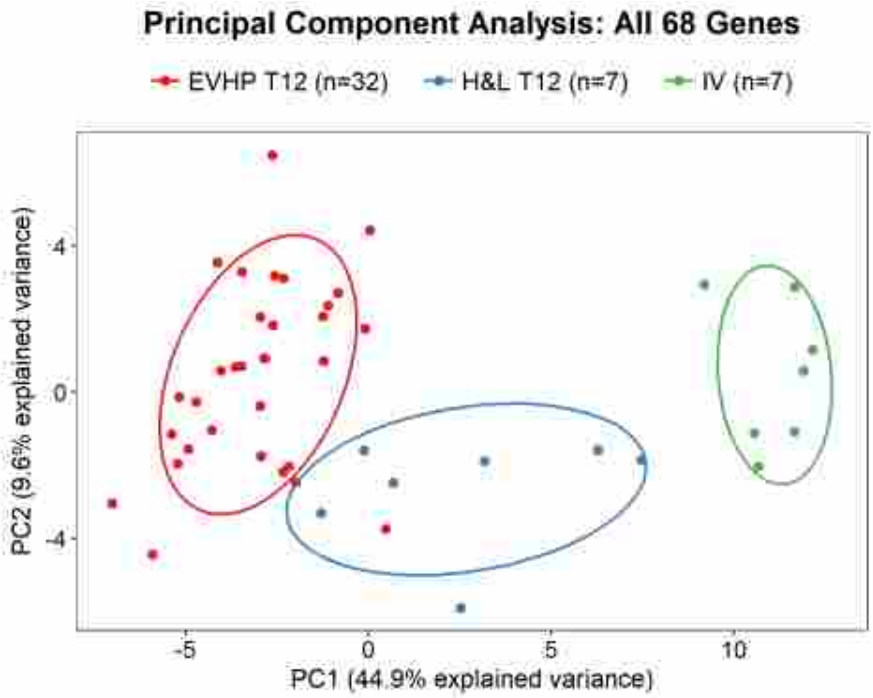
Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Cardiac transplantation is a life-saving intervention for advanced heart failure, but it is limited by a shortage of suitable donor organs. Ex vivo heart perfusion (EVHP) represents a promising alternative for organ preservation and repair. We aimed to assess the utility of gene expression for better understanding and monitoring cardiac injury and repair during EVHP. Methods: Biopsies were obtained from 46 porcine hearts either in vivo (IV, n=7) or after 12 hours of ex vivo heart (EVHP, n=32) or combined heart-liver (H+L, n=7) perfusion. Functional parameters were recorded during EVHP. Histology was assessed for features of cardiac injury. NanoString was used to measure 68 genes previously associated with cardiac injury and repair. Molecular data were assessed for differential expression and correlated with function and histology. Results: Principal component analysis demonstrated distinct clustering of sample groups based on gene expression patterns (Figure 1). 44 genes were significantly upregulated, and 12 genes were significantly downregulated in EVHP vs. IV (FDR < 0 .05). As aggregate gene sets, the upregulated and downregulated genes exhibited higher and lower expression, respectively, in EVHP vs. IV, EVHP vs. H+L, and H+L vs. IV ($p < 0.001$) (Figure 2). Gene set expression correlated with various functional parameters (Table 1) but not with histology. Conclusion: These data suggest that EVHP induces a molecular injury response that correlates with function. Interestingly, molecular injury appears reduced in combined heart-liver perfusion. This represents a novel approach for assessing the mechanism and extent of organ injury during EVHP.

Abstract Image 1:



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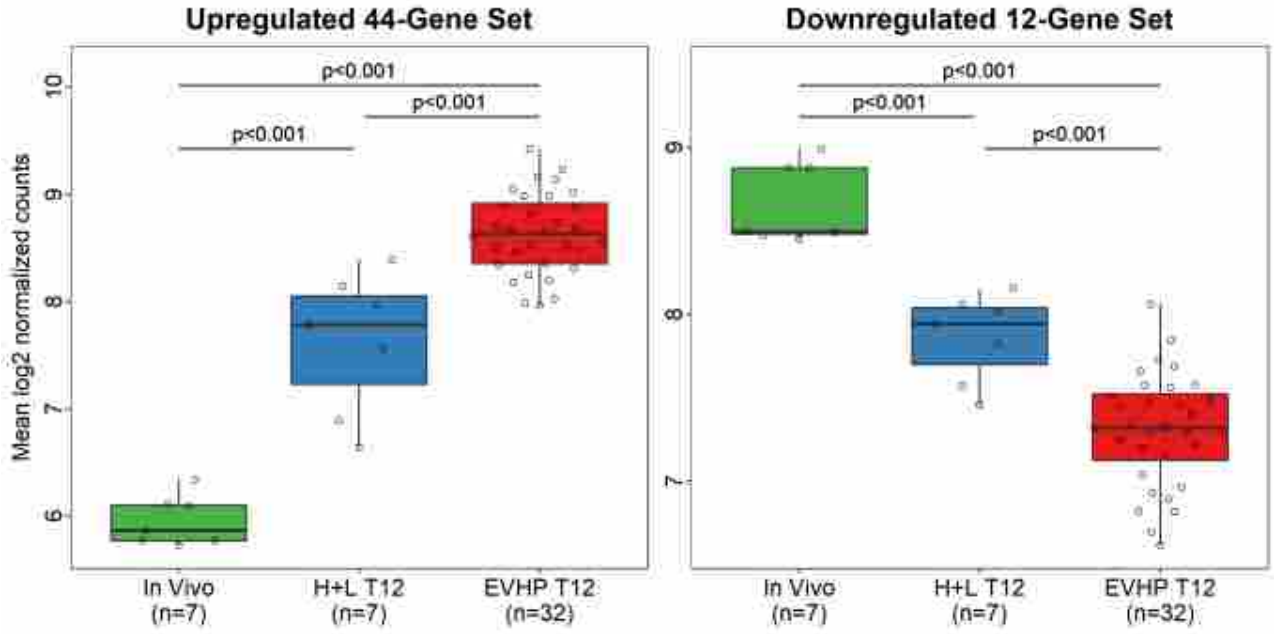
Abstract Image 2:



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Abstract Image 3:

Table 1: Correlation between gene set expression and functional parameters in 39 porcine hearts after 12 hours of ex vivo perfusion.

	Upregulated 44-gene set		Downregulated 12-gene set	
Functional Parameter	**r-value**	**p-value**	**r-value**	**p-value**
Weight gain (%)	0.101	0.553	-0.121	0.474
Cardiac index (ml/min/gram)	**-0.516**	**0.002**	0.073	0.681
Change in cardiac index (%)	**-0.626**	**<0.001**	-0.072	0.682
MVO2 (ml O_2/min/100g)	**-0.513**	**0.002**	0.260	0.143
Arterial lactate (mmol/L)	**0.640**	**<0.001**	**-0.549**	**<0.001**
Oxygen extraction (%)	**-0.612**	**<0.001**	**0.434**	**0.011**
Cardiac output (L/min)	**-0.523**	**0.002**	0.087	0.630
Stroke work (mmHg·ml)	**-0.623**	**<0.001**	0.250	0.167
Systolic pressure (mmHg)	-0.347	0.051	0.327	0.067
dP/dt_{max} (mmHg/s)	**-0.382**	**0.030**	0.174	0.341
dP/dt_{min} (mmHg/s)	**0.481**	**0.006**	-0.241	0.190

ID: 19
What attitude should we adopt with early graft failure in a recipient who participated in kidney paired donation?

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Living kidney transplantation offers the best medical outcomes for patients with end-stage renal disease. Living kidney donors have to be blood group and immunologically compatible with their recipients. Kidney paired donation (KPD) allows patients to circumvent the incompatibility obstacles by facilitating living kidney donation between patients with a willing but incompatible living donor and other pairs in the same situation by coordinating "kidney swaps" between incompatible pairs in Canada.. Participation in KPD for these incompatible pairs, accordingly, means that the kidney is from an anonymous and unknown donor who may be at a distance from the recipient. This means that the kidney could travel to the recipient transplant centres, thus increasing cold ischemia time, or that the donor has to travel to the recipient's transplant program. Early graft failure in the setting of KDP is rare and happens in less than 1%. In Canada, KPD is managed through the Canadian Blood Services (CBS) in coordination with the provincial and territorial organ donation organizations. Recently, a kidney recipient who participated in KPD unfortunately experienced early graft failure after his/her living donor had already donated to another recipient. This unfortunate situation raised the question of what, if anything, should be done with respect to, or is "owed to" this recipient, e.g., whether a priority for a kidney from KPD should be offered to this recipient with early graft failure in recognition of the fact that their living donor has participated in KPD. In this presentation, we will discuss the relevant ethics considerations regarding this question, including informed consent, justice, equity and medical utility. This analysis will also include consideration of the roles and responsibilities of transplant professionals and a coordinating agency (such as an organ procurement organization) with respect to donors and recipients when there is early graft failure.

DraftModeStatus: 0

ID: 20
A machine learning approach to predict tacrolimus level post-tacrolimus initiation after pediatric solid organ transplantation

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Member of: CDTRP

Abstract Type: Pediatric Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background There are significant challenges in achieving therapeutic tacrolimus levels after solid organ transplantation (SOT). We explored factors predicting tacrolimus levels post-transplant. Methods Pediatric SOT recipients were enrolled across 7 centers. Tacrolimus levels were captured at 36-48 hours post-tacrolimus initiation (T1) and serially for 1-year post-transplant. A linear mixed effect model was used to identify clinical factors associated with tacrolimus levels and genome-wide analysis to identify SNPs . To determine important predictors of T1 level, a machine learning approach was applied. Three random forest (RF) models were considered: clinical factors only, SNPs only, and clinical factors+SNPs. The importance of a variable was measured by the relative reduction in predictive accuracy when the variable was randomly permuted across observations. Regression tree was used to approximate the RF models with 3 most important variables. Results 455 recipients were included [median age at transplant, 4.5(1.0-11.7) years]. After adjusting for age, organ type, race, sex, tacrolimus dose and CYP3A4 inhibitor use, GWAS identified 25 SNPs associated with tacrolimus level ($p < 1$ 0-5), 8 at genome-wide significance ($p < 1$ 0-7) (Figure 1). An approximated RF model using 3 most important predictors of T1 levels i.e. organ type, dose and rs776746 is shown in Figure 2. In CYP3A5 non-expressors i.e. 0 minor allele for rs776746, organ type was an important predictor. Among CYP3A5 expressors i.e. 1/2 minor alleles, tacrolimus dose and organ type were important predictors. A model with clinical factors and SNPs had smaller prediction error than clinical or SNP alone models. Conclusion A machine learning approach identified the most important genetic and clinical factors predicting T1 level and showed that the dose-response of tacrolimus is influenced by genotype. RF modeling will help inform the development of organ and genotype-guided tacrolimus dosing.

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/20_AbstractImage2_0517091034.pdf

DraftModeStatus: 0

ID: 21
Sex and CD4 T cells are important factors in natural ABO antibody production in mice

Member of: CDTRP

Abstract Type: Pediatric Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: ABO-incompatible organ transplants (ABOi-Tx) are at high-risk of rapid rejection mediated by preformed ABO antibodies (Abs), except during infancy when these are absent. ABO Abs are produced 'naturally' in humans and mice without obvious exposure to ABH-antigens. Our group showed CD4 T-cells are needed to induce anti-A Ab production following immunization of wild-type (WT) mice with human A red blood cells (Hu A-RBC), however it remains unclear whether natural ABO Ab production is requires T-cell. Furthermore, sex is an important biological factor in immune responses and may also play role in ABO Ab production. Herein, we investigated the roles of sex, microbiome, and requirement of T cells for the production of natural ABO Ab. Methods (Table): WT and CD4, MHC-ii, and αβ/γδ T cell knock-out (KO) C57BL/6 (B6) mice received either i.p. injections of Hu A-RBC (weekly x3) or were untreated. Serum anti-A Ab was measured by hemagglutination assay. To study the role of gut bacteria in natural anti-A Ab production in CD4KO mice, drinking water was supplemented with antibiotics. Results (Table): WT B6 of both sexes produced increasing amounts of natural anti-A Ab with age. Compared to adult WT, female of all 3 KO strains developed significantly higher levels of natural anti-A Ab ($p \leq 0.001$). Female KO mice produced significantly higher natural anti-A compared to male mice. Hu A-RBC injection did not induce (or increase) anti-A production. Antibiotics significantly reduced anti-A production in CD4KO females. Conclusion: ABO Nabs can develop in the absence of CD4 T-cells, in contrast to induced Ab production which requires T cells. In addition, sex difference in all 3 KO strains with females producing markedly higher levels of natural ABO Abs than males. A role for the microbiome in generating Natural ABO Abs was suggested by a decrease in ABO Ab following antibiotic treatment.

Abstract Image 1:

Table

Treatment	Recipients	Age	Number	Anti-A Titer
Untreated	*WT* B6 females	6 – 10 weeks	8	4
Untreated	*WT* B6 males	6 – 10 weeks	7	2
Hu A-RBC injection	Female B6 *WT*	6 – 10 weeks	3	1024
Hu A-RBC injection	Male B6 *WT*	6 – 10 weeks	6	1024
Untreated	*CD4KO* females	6 – 10 weeks	7	1024 - 4096
Untreated	*CD4KO* males	6 – 10 weeks	3	16
Hu A-RBC injection	*CD4KO* females	6 – 10 weeks	7	1024 - 4096
Hu A-RBC injection	*CD4KO* males	6 – 10 weeks	5	16
Untreated	*MHC-ii* females	6 – 10 weeks	5	1024 - 4096
Untreated	*MHC-ii* males	6 – 10 weeks	3	16
Hu A-RBC injection	*MHC-ii* females	6 – 10 weeks	3	1024 - 4096
Hu A-RBC injection	*MHC-ii* males	6 – 10 weeks	4	16- 32
Untreated	*αβ/γδ T cells KO* females	6 – 10 weeks	3	1024 - 4096
Untreated	*αβ/γδ T cells KO* males	6 – 10 weeks	3	16- 32
Hu A-RBC injection	*αβ/γδ T cells KO* females	6 – 10 weeks	5	1024 - 4096
Hu A-RBC injection	*αβ/γδ T cells KO* males	6 – 10 weeks	5	16- 32
Antibiotics	*WT* B6	6 – 10 weeks	5	4
Antibiotics + Hu A-RBC injection	*WT* B6	6 – 10 weeks	5	256 - 512
Antibiotics *	*CD4KO* females	6 – 10 weeks	6	32
Antibiotics *	*CD4KO* males	6 – 10 weeks	10	4 - 8
Antibiotics * + Hu A-RBC injection	*CD4KO* females	6 – 10 weeks	9	32
Antibiotics * + Hu A-RBC injection	*CD4KO* males	6 – 10 weeks	5	8 - 16

*Antibiotics: 1g/L of neomycin, ampicillin, streptomycin, metronidazole and 0.25 g/L of vancomycin

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DraftModeStatus: 0

ID: 22
Transplant candidates' and transplant recipients' perspectives on the decision to accept or refuse an offer for a deceased donor kidney

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: The decision to accept or refuse a kidney from a deceased donor can be a difficult one. This study aims to capture the perspectives of transplant candidates and recipients on the decision-making process when a deceased kidney is offered for transplantation. Methods: We conducted five focus groups with 17 kidney transplant recipients (KTRs) and 17 transplant candidates (TCs) between November 2017 and December 2018. The discussions were digitally recorded and transcribed. The content of the interviews was analyzed using the qualitative thematic and content method. Results: Participants wanted to be informed of the deceased donor's characteristics and be involved in the decision-making process especially when an extended-donor criteria is offered. KTRs reported that the experience of being offered a kidney could be difficult because of the circumstances of the offer and unpreparedness to participate in the discussion. Both KTRs and TCs consistently trusted the allocation system and medical expertise when they received an offer for transplantation. To facilitate the decision-making process, patients reported that they would like to have some information on the expected survival time of the offered kidney and on wait time prolongation if the offer is declined. The interest for a decision assistance application for patient use was not high. Rather, patients expected transplant physicians to summarize the significant information that would impact graft survival time and explain it to them. Conclusion: TCs and KTRs felt unprepared but wanted to be involved in the decision to accept or not a deceased donor kidney. Tools that can help physicians communicate to TCs the expected graft survival time if an offer is accepted and wait time prolongation if it is refused could improve patient participation in the decision-making process.

DraftModeStatus: 0

ID: 23
Psychosocial risk factors and transplant suitability for patients with less than 6 months of abstinence: First year review of the Ontario ALD pilot program

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: BACKGROUND Patients with alcohol-associated liver disease (ALD) typically require 6 months of abstinence prior to being considered for liver transplant (LT). Though longstanding, there is ethical uncertainty and empirical inconsistency behind this practice. The ALD Pilot Program was initiated in Ontario in May 2018, allowing for patients with less than 6 months of abstinence to be referred for transplant. This previously excluded population is extensively assessed from a psychosocial perspective, including an examination of severity of alcohol use disorder, social support, psychiatric comorbidity, and other social determinants of health. METHODS All referrals were assessed by a multidisciplinary team, including social workers and addiction psychiatrists, to determine whether patients met the inclusion criteria developed for the Pilot Program. Psychosocial suitability for transplant was assessed using DSM-V criteria and the SIPAT tool, and sociodemographic information was recorded. RESULTS From May 2018 to May 2019, 224 patients were referred to the ALD program. 100 (45%) proceeded with initial psychosocial evaluation based on the program's criteria, while the remainder were declined. Length of initial abstinence ranged from none to over 24 months (average=4.3 months). A majority were male (76%) and Caucasian (83%), with an average age of 54.8. Half of the patients were married, and half were either actively employed or retired. All suitable protocol candidates demonstrated adequate social support and stable housing. Seventy-eight percent were declined for meeting criteria for severe alcohol use disorder, while some were unwilling to participate in relapse prevention (6%) or had significant psychiatric comorbidity (2%). CONCLUSION All patients accepted to the protocol had suitable social support and housing, a willingness to participate in relapse prevention treatment pre- and post-transplant and an absence of unstable psychiatric comorbidity. Long term follow up of these patients will continue to assess the value of these psychosocial factors when predicting successful transplant outcomes, rather than the "6 month rule" alone.

Abstract Image 1:

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Abstract Image 2:

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Abstract Image 3:

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DraftModeStatus: 0

ID: 24
Developing a standard protocol for ex-vivo extremity perfusion (EVEP)

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: The potential of extremity transplantation is critically limited by the 4--6 hours of preservation time currently offered by standard cold static preservation. Ex--Vivo Extremity Perfusion (EVEP) is an evolving platform striving to safely extend the preservation time of donated Vascularized Composite Allografts (VCA) allowing for greater applicability of upper limb transplants. There is yet to be optimization of EVEP protocols to determine ideal conditions for safe extended EVEP preservation times. Specifically, there remains controversy whether VCAs should be perfused at normothermia with a blood based perfusate or at hypothermia with an acellular perfusate during EVEP. Methods: Porcine forelimbs are perfused for 12 hours on a novel mobile ex--vivo perfusion system that was developed at our institution with a buffered extracellular perfusate with 25% bovine serum albumin. The EVEP protocols were stratified to limbs being perfused in either a hypothermia (10°C) group with acellular perfusate or a normothermia (38°C) group perfused with autologous packed red blood cells added to the perfusate (cellular perfusate). Parameters compared include histological analysis of muscle, compartment pressure, muscle response to electrical nerve stimulation, edema formation, and pro-inflammatory cytokine profiles. Results: Results indicate a significant difference in edema formation with the hypothermic conditions correlating with a greater weight gain (19.3±3.0% hypothermic group vs. 3.7±3.0% normothermic group, $p < 0.05$). At the end of perfusion, interstitial edema in muscle (% involvement) trended towards being significantly greater in the hypothermic group (33.3±20.7%) compared to the normothermic group (6.7±12.1%) (p=0.089). Significant differences in nerve stimulation, compartment pressure, cytokine profiles, and arterial pH were also observed between groups. Conclusions: A normothermic and cellular perfusate protocol suggest pre-clinical efficacy as the optimal conditions for extended EVEP compared to a hypothermic acellular protocol.

DraftModeStatus: 0

ID: 25
Predominant role of microvascular over tubular injury as driver of progressive renal damage and fibrosis post mild and severe acute ischemia-reperfusion injury

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Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ischemia-reperfusion injury (IRI) is a major risk factor for chronic renal failure. Here, we characterize the different cell deaths in tubular and microvascular compartments of IRI-induced acute kidney injury (AKI) and their relative importance in renal fibrogenesis. Methods: Unilateral renal artery clamping for 30 or 60 minutes with contralateral nephrectomy was performed in wild-type (C57BL/6) or caspase-3-/- mice. In vitro, human umbilical vascular endothelial cells (HUVECs) and human proximal tubular cells (PT2) were exposed to hypoxia-reoxygenation following caspase-3 silencing. Results: In the early stage of mild AKI (30 min model), caspase-3-/- mice showed aggravated tubular epithelial cell (TEC) with higher tubular injury scores and serum creatinine levels. Electron microscopy Receptor-interacting serine/threonine-protein kinase 3(RIPK3) immunohistochemistry, and phosphorylated RIPK3 levels demonstrated enhanced TEC necroptosis in caspase-3-/- mice. In contrast, microvascular congestion were reduced in early and extension phases in caspase-3-/- mice. In the long-term, microvascular rarefaction was reduced in caspase-3-/- mice. This was associated with reduced renal fibrosis, decreased α-smooth muscle actin (α-SMA) and collagen deposition within peritubular capillaries (PTC). Preservation of the peritubular microvasculature in caspase-3-/- mice led to reduced tubular ischemia, with lower hypoxia-inducible factor 1α (HIF1α) expression and improved tubular injury scores at long-term. In the severe AKI model (60 min model),despite similar initial tubular and microvascular injury, caspase-3-/- mice showed better long term outcomes: ameliorated tubular injury with lower tubular injury score, attenuated microvascular injury with reduced microvascular congestion, as well as reduced collagen deposition and reduced α-SMA within PTC. In vitro,caspase-3 silencing significantly decreased apoptosis in HUVECs but increased necrosis in PT2 cells submitted to hypoxia-reoxygenation treatment. Conclusions: Collectively, these results establish the pivotal importance of caspase-3 in regulating microvascular apoptosis and fibrosis post-IRI. These findings also demonstrate the predominant role of microvascular over tubular injury as a driver of progressive renal damage and fibrosis post IRI.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/25_AbstractImage1_0514041227.pdf

DraftModeStatus: 0

ID: 26
HLA eplet frequencies reduce genetic complexity and provide the foundation for a national eplet-matching program in kidney transplantation.

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND: This study presents the HLA allele and eplet frequencies in patient and donor populations in BC to explore the likelihood of matching by each method as a foundation for a national eplet-matching program for kidney transplantation. METHODS: Next Generation Sequencing was performed in 1846 patients and donors for all 11 classical HLA genes. Alleles were converted to eplets with HLAMatchmaker, and frequencies were compared across donor and patient groups using statistical models and k means clustering. RESULTS: 361 alleles were identified (206 class I, 155 class II) and translated to 148 eplets (59 class I, 89 class II), a 59% reduction in complexity. There was a complex relationship between alleles and eplets (Image1): eplet 193PV was encoded by 51 alleles whereas B*07:02 allele encoded 6 eplets. Allele frequencies across all 4 groups of transplanted patients (KTx), pre-transplant patients (KPre), living donors (LD), and deceased donors (DD) were lower than eplet frequencies (Image2). Only one allele (DPA1*01:03) occurred in more than 48% of subjects, whereas eplet frequencies were more homogeneous, with some eplets occurring in >98% of subjects (i.e. 85VG). Overall allele frequencies differed significantly between patient and donor groups (p CONCLUSION: Even in the highly ethnically diverse population of BC, eplet typing markedly reduces the complexity of HLA identity by comparison with allele typing. Eplet frequency profiles are comparable between patient and donor populations, and subdivide into a small number of principal clusters. These results suggest that eplet typing may simplify histocompatibility matching for kidney transplantation.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/26_AbstractImage1_0602100628.pdf

Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/26_AbstractImage2_0602100629.pdf

Abstract Image 3: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12578/26_AbstractImage3_0602100630.pdf

DraftModeStatus: 0

ID: 28
Persistent atelectasis following primary graft dysfunction is associated with lower lung function in lung transplant recipients

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Primary graft dysfunction (PGD) is a major contributor to mortality and impaired lung function in lung transplant recipients. We assessed radiographic features on post-transplant lung computed tomography (CT) scans and their association with long-term lung function. We hypothesized that radiographic abnormalities would be more frequent in PGD survivors and mediate poorer lung function. We studied double-lung transplant recipients at the University of Alberta Hospital from 2010-2016. Grade 3 PGD (PGD3) was defined by lung edema and PaO2/FiO2 237 patients met inclusion criteria, 50 of whom developed PGD3 at 48 or 72h. PGD3 was associated with more frequent/widely distributed interlobular septal thickening (p=0.0389) and atelectasis (p Grade 3 PGD is associated with atelectasis at 3-month post-transplant, and this atelectasis appears to be a mediator of lower lung function at 1-year in PGD survivors. This may suggest persistent surfactant and type-II pneumocyte dysfunction in post-PGD lungs.

DraftModeStatus: 0

ID: 29
Natural killer cells and mitochondrial damage-associated molecular patterns in ischemia reperfusion injury during liver transplantation

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Member of: CDTRP

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Tissue damage and necrotic cell death following ischemia reperfusion injury (IRI) during liver transplantation (LT) compromise cellular integrity and lead to release of damage-associated molecular patterns (DAMPs). DAMPs of mitochondrial origin (mitoDAMPs) incite profound inflammation following tissue damage and ischemia (Figure 1). This is salient in LT as 1) the liver is acutely sensitive to hypoxia, and 2) has a high mitochondrial content. MitoDAMPs serve as a biomarker to predict clinical outcomes in a variety of disease processes, and higher mtDNA levels in donor plasma are correlated with early allograft dysfunction (EAD) in LT recipients. Natural killer (NK) cells, immune cells of the lymphoid lineage, are involved in IRI-mediated inflammation, but whether their contributions are beneficial or protective is controversial. We have recently determined that mitoDAMPs drive NK cells toward an immune-tolerizing role (Figure 2). We hypothesize that 1) mitoDAMPs polarize NK cell function towards immunoregulation during IRI and 2) mtDNA levels in perfusate collected during ex vivo normothermic machine perfusion will be predictive of EAD, as well as graft and patient survival following LT. Methods: In vitro study of primary NK-mitoDAMP interaction, assessed via ELISA and FACS analysis of human and murine NK cells. In parallel studies, qPCR is being used to quantify mitoDAMPs in perfusate samples. Results: MitoDAMPs suppress NK cell activation in a dose-dependent manner: they diminish inflammatory cytokine production and incite IL-10 release. NK cells treated with mitoDAMPs are actively regulatory and suppress proliferation of autologous T cells. Pilot studies have revealed that mtDNA in perfusate samples can be successfully isolated and quantified. Data collection and analysis of clinical outcomes are ongoing. Conclusion: NK cell function and the concentration of mitoDAMPs in liver perfusate could inform the expected course of disease and assist in strategies to ameliorate inflammation by promoting tolerogenic features of NK cells.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/29_AbstractImage1_0529093247.pdf

Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/29_AbstractImage2_0529093248.pdf

DraftModeStatus: 0

ID: 30
PUBLIC SOLICITATION FOR A LIVING KIDNEY DONOR: EFFECTS ON THE TRANSPLANT WAITING LIST AND HLA LABORATORY WORKLOAD

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction: Solicited organ donation offers the opportunity for patients with end-stage renal disease to identify a living donor, typically when one might not exist in their family or friend network. Solicited donation raises ethical issues and can also have a significant impact on workload in the histocompatibility laboratory. Methods: A 42 year-old patient was a candidate for a second transplant following failure of his first graft, 15 years post-transplant. In February 2018, his spouse solicited living donors using billboard advertising and a prominent social media platform; various news outlets also reported the story of this search. The transplant program received about 170 phone inquiries, 50 people agreed to proceed to HLA testing, and medium resolution HLA typing was ultimately performed on 25 people. Sixty-four percent (16/25) of these potential donors were female, with a median age of 45. Results: The patient was highly sensitized (cPRA 95%), and 25 virtual crossmatches were performed. Eighty-eight percent (22/25) of these were positive, and two prospective donors with a negative virtual crossmatch proceeded to a preliminary and final flow crossmatch that was compatible. The patient received a kidney in November 2018 and the most recent single antigen results showed positivity against DR8 only with a cPRA of 7; no DSA was detected. Four potential donors have transferred to donor programs in other provinces, one donor is currently in workup for a specific local recipient, and one potential donor's workup is on medical hold. If these transplants proceed, 6 additional patients will receive a new kidney. Conclusions: As the trend of solicited donation increases, clinical departments need to address the potential increase in workload, and potential donors should be encouraged to consider anonymous non-directed organ donation within the context of Canada's National Kidney Paired Donation program to maximize the number of patients benefitting from altruistic donation.

DraftModeStatus: 0

ID: 31
Partnerships Between Patients and Researchers within the Canadian National Transplant Research Program : changing practices and influencing research from priorities onwards

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background Patients partners are active members of the Canadian National Transplant Research Program (CNTRP), both at the research teams, network and project levels. This evaluation aimed to assess prospectively the patient-researcher partnership within the CNTRP and document how it affected projects, studies and partners. Methods We conducted 13 semi-structured interviews with 17 partners (researchers and patients). The interviews were digitally recorded and transcribed. Thematic and content analysis was conducted. Results There has been a change in research practices and management within CNTRP. These changes are related to an increased presence of patients and continuous exchange on several levels. Engagement evolved as collaborative work progressed to gradually move from consultation to co-design. Researchers engaging with patients report that they see clearer links between their research projects and healthcare outcomes, and that involving patients transformed research communication. Several researchers mention their desire to continue conducting research projects in partnership with patients as co-investigators in the future, justifying this choice by the relevance it gives to their research and the changes in direction that bring them closer to the patients and caregivers journey. The CNTRP's partnership governance has enabled the continuity of partnership approaches, an increase in partners' capacities, as well as a validation of practices through the dissemination of a common vision of research in partnership with patients and the public. Conclusion This study documents the impact and experience of patient-researcher partnership within the CNTRP at different stages and levels of research. The results of this study allowed us to develop tools and define the winning conditions for future partnership in research in transplantation and organ donation in Canada.

DraftModeStatus: 0

ID: 32
Acceptance, safety and effectiveness of exercise interventions in solid organ transplant candidates: a systematic review

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Exercise training may be recommended to solid organ transplant (SOT) candidates to improve fitness and tolerance for the upcoming physiologic stressor (surgery). We systematically reviewed the literature to 1) determine the acceptance and safety of exercise interventions in SOT and 2) examine the effect of these interventions on exercise capacity and quality of life (QoL) in this population. Methods: Online databases were searched. Studies of any design were included. Outcomes of interest were acceptance, safety, maximal and/or functional exercise capacity and QoL. Results: Twenty articles were included (n=1765patients). All organs except pancreas were represented. The exercise interventions ranged from 4 to 25 weeks and offered aerobic and/or strength exercises. An average of 80% of the approached patients in the included studies agreed to participate in the exercise interventions.Thirteenstudies assessed adverse events and one reported four minor medical complications.Three out of five studies that assessed maximal exercise capacity reported an increase in this outcome in the intervention group post-exercise (mean change ranged from 0.69 to 2.5mL/kg). Seven out of twelve studies reported an increase in 6-minute walking distance in the intervention group after the training period (mean change ranged from 40 to 100 meters). Seven articles reported the SF-36 mental and physical composite scores. Only one article showed an improvement in the mental composite score (mean change: 8.7±13.5 points) and three articles showed an improvement in the physical composite score (mean change ranged from 1.9 to 3.6 points) in the intervention group. Conclusion:The majority of the approached patients accepted to participate in an exercise intervention pre-transplant. There is some evidence that exercise training is safe and can improveexercise capacity in SOT candidates. There is poor evidence for the effects of exercise on the mental and physical aspects of QoL in this population.

DraftModeStatus: 0

ID: 33
BRIC STUDY - BURNOUT AND RESILIENCY LEVELS AMONG ORGAN DONATION COORDINATORS: RESEARCH PROTOCOL

Member of: CDTRP

Abstract Type: General Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background Numerous research studies have highlighted the importance of the organ and tissue donation coordinator (OTDC) to the success of organ donation3-7, 10. However, facing challenging and stressful scenarios on a daily basis often leads to burnout, attrition, and compassion fatigue among OTDCs7-9. Unfortunately, for some OTDCs, coping with emotions and quality expectations is overwhelming and they may resign in less than 3 years7, 9. Increased turnover rates of OTDCs would likely have significant impact on the ability of Organ Donation Organizations to optimize donation. We are proposing an innovative way of dealing with burnout: identifying and intervening in the causes to avoid losing experienced and exceptional OTDCs. Methods Phase 1: a Joanna Briggs Institute systematic scoping review will be conducted to answer the question: What experiences of burnout, compassion fatigue, and/or attrition among OTDCs worldwide have been reported? Phase 2: a mixed-method study based on the scoping review results will be conducted to identify the extent of the problem among Canadian OTDCs. Phase 3: an interventional study will be developed and implemented to address the main issues faced by OTDCs in Canada. Methods overview: figure 1. Expected Results Phase 1 will generate findings about burnout and turnover among coordinators worldwide. Phase 2 will determine unknown characteristics and extent of this issue in Canada. Phase 3 will contribute to the healthcare system by improving OTDCs mental health and, consequently, the quality of organ donation processes. Conclusion The findings generated by this three-step study will inform the creation and implementation of tailored interventions to address the issue. Interventions will ease the burden felt by OTDCs and help them strive professionally/emotionally, consequently reducing turnover rates. Less burnout and turnover will result in more experienced and satisfied staff, leading to more donors and better experiences by families approached to consent for donation.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/33_AbstractImage1_0515065454.pdf

DraftModeStatus: 0

ID: 34
BURNOUT AND RESILIENCE AMONG ORGAN DONATION COORDINATORS: SCOPING REVIEW PROTOCOL

Member of: CDTRP

Abstract Type: General Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background Research has shown that organ and tissue donation coordinators (OTDC) face challenging and stressful scenarios daily, leading often to burnout, attrition, and compassion fatigue1-3. Unfortunately, coping with those scenarios is overwhelming and OTDCs may resign in less than 3 years2, 3. Increased turnover rates of OTDCs would likely have significant negative impact Organ Donation Organizations' optimization of donation. Therefore, as part of a national three-phase study, this scoping review aims to understand the nature of burnout problem worldwide and inform the development of following studies to identify and intervene in the causes to avoid losing experienced and exceptional OTDCs. Research question: What experiences of burnout, compassion fatigue, and/or attrition among Organ and Tissue Donor Coordinators worldwide have been reported? Methods Systematic scoping review protocol in accordance with the Joanna Briggs Institute (JBI): Title/protocol registration followed by a three-step search strategy (figure 1) on PUBMED, CINAHL, EMBASE, LILACS) and grey literature (Organ donation association websites, Google Scholar (first eight pages), Research Gate, and consultation of international researchers and associations in organ donation field). Inclusion criteria:Documents reporting burnout syndrome, moral distress, attrition, or compassion fatigue, grief, trauma, vicarious trauma, secondary trauma, conflict, anxiety, psychological distress, PTSD, depression, resilience processes, and consequences of stress among OTDCs, full text in Spanish, Portuguese, French or English, no year limit. Data synthesis:quantitative analysis (e.g., frequency analysis) of general data on the type of study, country of study, etc.; and qualitative analysis (e.g. thematic analysis) of the components of the research purpose and conceptual findings regarding burnout, compassion fatigue, attrition and its consequences among OTDCs. Expected Results This study will generate findings about burnout and turnover among coordinators worldwide. Conclusion This review results will inform the development of a research question, and the best methodology for the next phase of this national study.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/34_AbstractImage1_0515070200.pdf

DraftModeStatus: 0

ID: 35
Management of Post Kidney Transplant Leukopenia: A Practical Algorithm and Outcomes at a Single Center

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

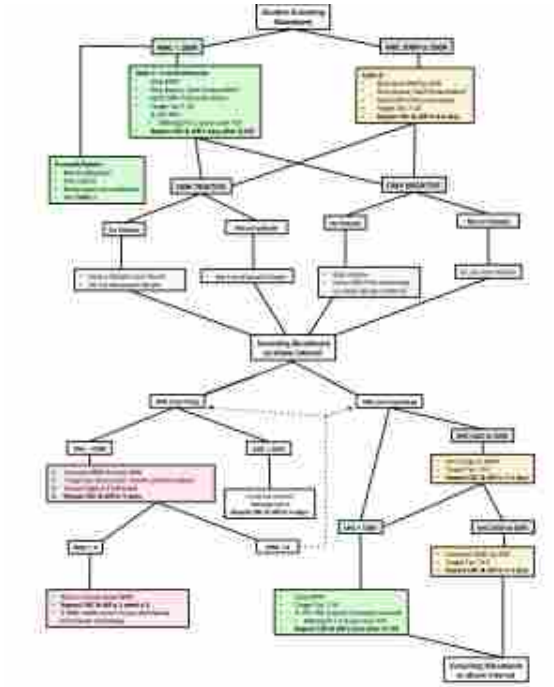
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Leukopenia (defined as a white blood count (WBC) < 3.5) occurs frequently following kidney transplantation and may be associated with adverse clinical outcomes including increased infectious risk. Reducing immunosuppression in response to leukopenia may lead to transplant rejection and graft loss. Methods: We conducted a retrospective analysis of patients ≥ 18 years of age who developed post-kidney transplant leukopenia (PKTL) in our clinic from Jan 2016 to Dec 2018 with ≥3 months of follow-up. Our objective was to determine if a PKTL management algorithm (instituted in our transplant clinic January 2017, Figure 1) improved patient results over time (comparing 2016 outcomes (pre-algorithm) with 2018 outcomes (post-algorithm)). We evaluated the total duration of leukopenia, nadir WBC and absolute neutrophil count (ANC), days with mycophenolate mofetil (MMF) held, and the need for granulocyte colony stimulating factor (G-CSF) rescue therapy in 2016 versus 2018. Comparisons were performed using the student paired t-test, Wilcoxon Signed Rank test, or chi-squared test as appropriate. Results: 8 patients developed PKTL in both 2016 and 2018. The median duration of leukopenia was 37 days (IQR 31-43) in 2016 versus 12 days (IQR 9-26) in 2018 (p-value 0.005). Median nadir WBC (1.45 (IQR 1.3-2.4)) and ANC (325 (IQR 230-515)) in 2016 were significantly lower than in 2018 (nadir WBC 2.7 (IQR 2-3) and ANC 930 (IQR 390-1270)), p-value 0.034 for both comparisons. There was no significant difference in total days with MMF held in 2016 versus 2018. In 2016, G-CSF was used as rescue therapy in 4 of 8 leukopenic patients (50%) compared with no patients requiring G-CSF in 2018 (p-value 0.008). There were no significant differences in adverse outcomes associated with PKTL or PKTL management in 2016 and 2018. Conclusion: Institution of a practical algorithm for the management of PKTL improved patient outcomes from 2016 to 2018.

Abstract Image 1:



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DraftModeStatus: 0

ID: 36
Post-Kidney Transplant Leukopenia: Predictors and Complications

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Leukopenia occurs frequently following kidney transplantation and has been associated with adverse clinical outcomes including increased infectious risk. In this study, we sought to identify predictors of post-kidney transplant leukopenia (PKTL) and to explore the association of leukopenia with adverse outcomes including the risk of infectious complications, transplant rejection, graft failure, and death. Methods: We conducted a retrospective study of adult patients (≥ 18 years of age) who received a solitary kidney transplant at a single tertiary care center from January 1, 2006 to December 31, 2017. The primary outcome was time to PKTL defined as a white blood count (WBC) < 3.5. We identified factors associated with PKTL using Cox multivariable hazards models and backwards stepwise selection of variables significantly associated with the outcome of interest in unviariable analysis at a p-value of < 0.05. Results: A total of 152 (39.2%) patients (out of the 388 transplanted) developed PKTL. Antithymocyte globulin induction therapy (versus Basiliximab) (HR 3.32, 95% CI 2.25-4.91), prophylactic use of Valganciclovir (HR 1.60, 95% CI 1.08-2.38), pre-transplant blood transfusion (HR 1.16, 95% CI 1.09-1.25 per unit of blood), and choice of calcineurin inhibitor (Tacrolimus versus Cyclosporin) (HR 3.05, 95% CI 1.08-8.55), but not anti-proliferative agent were all independently associated with the development of PKTL. The discriminative ability of the generated multivariable model to predict PKTL was reasonable (c-statistic 0.73, 95% CI 0.68-0.78). The only adverse outcome significantly associated with the development of PKTL was CMV viremia (HR 2.7, 95% CI 1.4-5.0 in those with versus without leukopenia) which occurred a median of 24.5 days (Q1, Q3: 0, 64) after PKTL. Conclusion: This study confirms that the prevalence of PKTL is high (39.2%) with the most significant predictors of PKTL being induction and maintenance immunosuppression strategies. PKTL is associated with an increased risk of CMV viremia.

DraftModeStatus: 0

ID: 37
Total parenteral nutrition in ex vivo lung perfusion: addressing metabolism improves both inflammation and oxygenation

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ex vivo lung perfusion (EVLP) protocols generally limit metabolic supplementation to insulin and glucose. Furthermore, conventional perfusates are void of many ingredients considered essential for cellular viability. We sought to determine whether the addition of total parenteral nutrition (TPN) would improve lung function in EVLP. Methods: Ten porcine lungs were perfused using EVLP for 24 hours and supplemented with insulin and glucose. In the treatment group (n=5), the perfusate was also supplemented with a continuous infusion of TPN containing lipids, amino acids, essential vitamins and cofactors. Physiologic parameters and perfusate electrolytes were continuously evaluated. Perfusate lactate, lipid and branch chain amino acid (BCAA) concentrations were also analyzed to elucidate how substrates were being utilized over time. Results: Lungs in the TPN group exhibited significantly better oxygenation. Perfusate sodium was more stable in the TPN group. In the control group, free fatty acids (FFA) were quickly depleted, reaching negligible levels early in the perfusion. Alternatively, BCAA in the control group rose continually over the perfusion demonstrating a shift towards proteolysis for energy substrate. In the TPN group, both FFA and BCAA concentrations remained stable at in vivo levels after initial stabilization. TNF-α concentrations were lower in the TPN group. Conclusion: The addition of TPN in EVLP allows for better electrolyte composition, decreased inflammation, and improved graft performance.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/37_AbstractImage1_0516114737.pdf

DraftModeStatus: 0

ID: 38
Initial successful clinical transplantation using negative pressure ventilation ex vivo lung perfusion with extended criteria donor lungs

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND: Ex vivo lung perfusion (EVLP) has been shown to successfully increase the use of extended criteria donor (ECD) lungs in transplantation. Negative pressure ventilation EVLP (NPV-EVLP) has been described pre-clinically to be associated with decreased ventilator-induced lung injury compared to positive pressure ventilation EVLP. We report the first clinical experience utilizing NPV-EVLP for the assessment, preservation, and transplantation of ECD lungs. METHODS: Between October and February 2019, 7 patients were transplanted using extended criteria donor lungs following NPV-EVLP. Lungs were flushed with low-potassium dextran solution prior to explant. Following return to the centre of implantation, they were connected to the NPV-EVLP system and perfused for between 2-6 hours. Lungs were perfused with a combination of Steen solution and red blood cell concentrate. Donor and recipient characteristic assessed included ECD lung scores, Primary Graft Dysfunction (PGD) scores at 0, 24, 48, and 72 hours, time to extubation, length of ICU and hospital stay, requirements for extracorporeal membrane oxygenation (ECMO), and graft and patient survival. RESULTS: All grafts and patients survived to 30 days and recovered to discharge from hospital. There were no patients with PGD 3 at 72 hours post-op. The average pre-procurement donor P:F ratio was 245 ± 49 mmHg. The average final P:F ratio on NPV-EVLP was 433 ± 35 mmHg. The mean time on EVLP was 176 ± 12 min. The average duration of mechanical ventilation was 30 ± 6 hours. The average ICU length of stay was 5.3 0.7 days. No patients required ECMO post-operatively. CONCLUSION: Negative Pressure Ventilation Ex Vivo Lung Perfusion demonstrates safe preservation, evaluation, and successful clinical transplantation of extended criteria donor lungs. Further validation of this initial cohort is ongoing, including the development of a portable device for multi-centre international clinical trials.

DraftModeStatus: 0

ID: 39
The effect of left ventricular assist devices (LVAD) on pulmonary hypertension in end-stage heart failure: a multicenter study

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background Despite the increasing prevalence of advanced heart failure, transplantation rates have remained stable in Canada due to limited organ availability. Consequently, the number of implanted left ventricular assist devices (LVAD) and average time on device support have both risen rapidly. End-stage heart failure is often complicated by pulmonary hypertension (PHTN). Patients with PHTN have historically not been candidates for transplantation but reports of PHTN reversibility with LVAD support have led to changes to ISHLT listing criteria which now state that pulmonary hemodynamics should be reassessed 3 to 6 months following LVAD implantation for PHTN reversibility and transplantation candidacy. Methods All patients having received a permanent LVAD at two transplantation institutions were included in our study. Pre-operative characteristics were obtained from institutional databases. Right-heart catheterization data was retrospectively retrieved for 90 days pre-insertion and up to 3 years post-insertion. Pulmonary vascular resistance (PVR) was calculated for each instance from the transpulmonary gradient and cardiac output. Generalized estimating equation was used to determine if any variable was associated with PHTN reversibility. Results 214 patients for a total o 655 hemodynamic measurements were captured and their peri-operative characteristics are summarized in Table 1. Patients with pre-operative PHTN (defined as a pre-operative PVR > 3 Wood Units) were less likely to have an ischemic etiology but were otherwise similar to the normotensive cohort. Longitudinal PVR measurements for patients with and without pre-operative PHTN are visualized in Figures 1 and 2. The majority had normalization of their PVR 6 months post-operatively. Generalized estimating regression revealed that pre-operative PVR was the only variable significantly associated with subsequent changes in PHTN. Conclusion In our study, LVAD use led to reversibility of PHTN for the majority of patients within 6 months. With the exception of pre-operative PVR, no other variable was significantly associated with PHTN reversibility.

Abstract Image 1:

Variable			PHTN	No PHTN	P Value
Total patients		n (%)	107 (50.0)	107 (50.0)	
Age		years	52.3 ± 13.3	51.4 ± 13.2	0.63
Smoking history		n (%)	48 (48.5)	53 (51.9)	0.62
Hypertension		n (%)	51 (51.5)	41 (40.2)	0.11
Diabetes		n (%)	35 (35.4)	29 (28.4)	0.29
Dyslipidemia		n (%)	72 (72.7)	64 (62.6)	0.13
Renal Insufficiency		n (%)	16 (36.4)	24 (42.9)	0.51
EF		%	18.7 ± 7.3	18.3 ± 6.8	0.63
Ischemic Cardiomyopathy		n (%)	26 (26.3)	41 (40.2)	0.04
LVAD	**PVAD**	n (%)	4 (3.7)	8 (7.5)	0.61
	XVE	n (%)	1 (0.9)	2 (1.9)	
	HM2	n (%)	59 (55.1)	63 (58.9)	
	HVAD	n (%)	25 (23.4)	18 (16.8)	
	HM3	n (%)	17 (15.9)	14 (13.1)	

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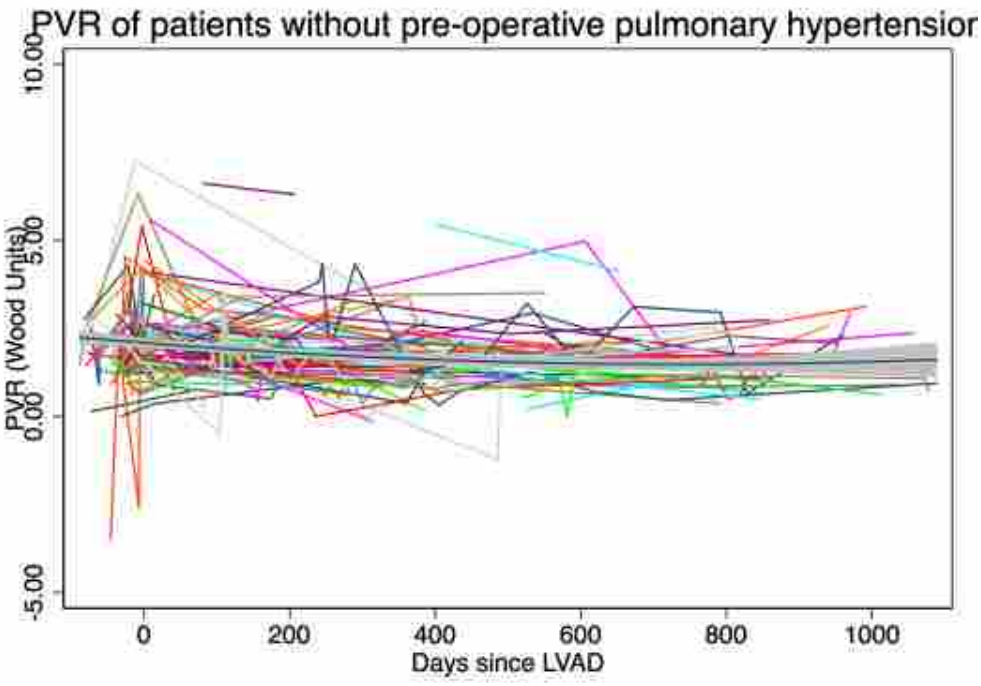

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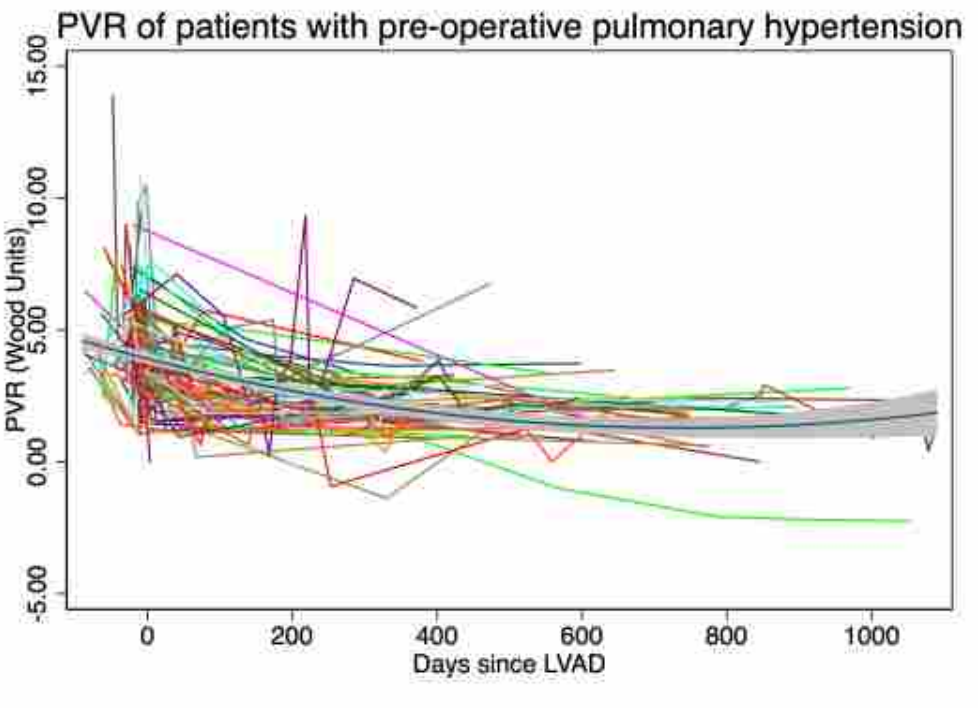

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DraftModeStatus: 0

ID: 40
The impact of reduction of warm ischemia removing the second warm ischemic period on DCD kidney transplantation outcomes

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Warm ischemic time (WIT) during DCD kidney transplantation has significant effects on post-operative outcomes, such as graft survival, function, and post-operative mortality and morbidity. As second WIT also occurs while the kidney rewarms during the anastomosis (WIT2). We applied cooling effect using an the ice blanket technique (IBT) to see if eliminating WIT2a second WIT (WIT2) would will decrease the incidence of DGF and improve renal functional outcomes. Methods: Adult DCD kidney transplants performed at our center b/w 2017 and 2018 were reviewed (N=32). Transplants were performed as standard and in ice blanket group. A comparison was done in regards to total WIT b/w a group that received the IBT (N=17) and those that received transplants without ice blanket (non-IBT, N=15). Outcomes included DGF and post-operative renal function. Results: Demographic characteristics were not different b/w the groups. There was no difference in procurement WIT (WIT1) or cold ischemic times b/w the two groups ($p = 0.58$ and $p = 0.19$).Both groups were followed up for 3 months period. Donor and recipient demographics were similar. Standard criteria donors and expanded criteria donors comprised about 70% and 30% in both groups. By definition, overall WIT (WIT1+2) was greater in the IBT group. 17 of the 32 patients underwent transplantation using IBT. On days 1, 3, and week 4, IBT grafts had superior renal function vs. non-IBT ($p < 0.05$). Although there was no difference in DGF b/w groups, the median number of dialysis sessions was 2 (2-3) in the IBT and 4 (2-6) in the non-IBTS groups. Slow graft function rates were higher in the non-IBTS group, accordingly. Conclusion: Decrease in overall WIT using IBT improved renal function and slow graft function. This is a preliminary study with ongoing data collection and larger studies with IBTwill be necessary in order to truly determine improved outcomes.

DraftModeStatus: 0

ID: 41
Comparison of centrifugal and pulsatile perfusion to preserve donor kidneys using ex vivo subnormothermic mechanical perfusion

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: We have previously demonstrated benefits of kidney preservation utilizing an oxygenated sub-normothermic ex vivo perfusion platform. Herein, we aim to compare pulsatile versus centrifugal perfusion with the goal of optimizing renal preservation with this device. Methods: Pig kidneys were procured following 30 min of warm ischemia by cross-clamping both renal arteries. Paired kidneys were cannulated and underwent either: oxygenated pulsatile or centrifugal perfusion using a hemoglobin oxygen carrier at room temperature with our ex vivo machine perfusion platform for 4hr. Kidneys were reperfused with whole blood for 4 hours at 37º C. Renal function, pathology and evidence of inflammation were assessed post-perfusion. Results: Both pump systems performed equally well with organs exhibiting similar renal blood flow, and function post-reperfusion. Histologic evidence of renal damage using apoptosis staining and acute tubular necrosis scores were similar between groups. This was corroborated with urinary assessment of renal damage (NGAL) and inflammation (IL-6), as levels were similar between groups. Conclusion: In our donation after cardiac death renal transplant porcine model, pulsatile perfusion yielded similar renal protection compared with centrifugal kidney preservation. Both methods of perfusion can be used in ex vivo kidney perfusion systems.

DraftModeStatus: 0

ID: 42
Soluble C-Type Lectin Receptor Protein Inhibition of Natural Killer Cell Mediated Tubular Epithelial Cell Death

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: We have previously shown that Natural Killer (NK) cells can mediate kidney tubular epithelial cell (TEC) death, kidney ischemia-reperfusion injury (IRI) and chronic transplant rejection. MHC-independent mechanisms such as binding of NKRP1 receptors to C-type lectin receptor (Clr) family proteins, may regulate NK cell function. TEC can regulate NK cell activation and cytotoxicity by their expression of inhibitory Clrs, which we have now produced in genetically altered tobacco. Methods: Expression of Clr-b and Clr-f was confirmed in TEC using RT-PCR. WT and Clr-b-/- TEC were treated in vitro with Clr-f siRNA. Cell death was measured in NK-TEC co-cultures by 51Cr release assay. To obtain Clr-b, Clr-f, and Clr-b+f fusion protein, we designed and synthesized a codon-optimized Clr-b, -f, and fusion genes according to the frequency of codon usage in tobacco. The genes were then cloned into plant viral expression vectors and transiently expressed in tobacco plants. The expression of proteins was confirmed by immunoblotting and the expressed Clr proteins were purified using nickel affinity chromatography. Results: Clr-b and f expression in TEC was upregulated by TNFα+IFNγ treatment in vitro. Elimination of either Clr-b or Clr-f alone in TEC did not increase NK mediated killing. However, silencing of both Clr-b and Clr-f expression resulted in increased NK killing of TEC (n=3, p Conclusions: Our data support that NKRP1-Clr binding is an important inhibitory pathway in NK mediated kidney injury. As no current drugs target NK cells effectively, Clr-b/Clr-f proteins may represent a novel strategy to inhibit NK-mediated injury of kidneys in IRI and post-transplant. Indeed, plant-expressed Clr proteins may represent a class of NK directed therapeutics to protect organs from diverse forms of NK mediated inflammation and cytotoxicity.

DraftModeStatus: 0

ID: 43
Evidence of alveolar epithelial alterations associated with ischemia/reperfusion injury and primary graft dysfunction in lung transplants

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ischemia reperfusion injury (I/R) is the major cause of primary graft dysfunction (PGD) after lung transplantation. I/R and PGD feature endothelial/alveolar epithelial damage, lung edema and inflammation. Edema resorption then depends on the restoration of alveolar epithelial integrity and the ability of alveolar cells to reabsorb Na+ (through ENaC channels) and fluid. We hypothesized that alveolar epithelial damage, and repair, are critical in PGD pathophysiology, and resolution. Therefore, our aim is to identify novel biomarkers and therapeutic targets associated with I/R using cellular and animal models as well as human samples from lung transplants. Methods: The impact of a protocol mimicking hypothermic ischemia and reperfusion was first tested on primary rat alveolar epithelial cell cultures. Then, an inflammatory stress was induced by LPS in a porcine model of ischemia/ex-vivo reperfusion. Finally, lung biopsies from the donor grafts were collected during lung transplantations and the PGD score within the recipients were then determined. Results: In primary cell cultures, we showed altered ENaC and tight junction protein (ZO-1) expression following the I/R mimicking protocol. A decline in transepithelial resistance and reduced alveolar wound repair rates were also observed. Treatment with a KvLQT1 K+ channel activator (R-L3) accelerated the repair rates and enhanced barrier integrity (ZO-1 staining) and ENaC protein expression. In the porcine model, alveolar damage, lung edema, exacerbated inflammatory response and decreased ENaC expression were observed. Preliminary data from lung transplant samples indicated an inflammatory response and decreased ENaC and ZO-1 expression in the donor graft among patients subsequently developing a PGD. Conclusion: Our data support the hypothesis of alveolar epithelial dysfunction after I/R injury. We will now investigate a potential correlation between levels of inflammatory molecules and epithelial damage markers in bronchoalveolar lavages and blood samples (at different time-points) from lung transplants with various PGD scores.

DraftModeStatus: 0

ID: 44
Developing a Canadian eplet-matching program: Precision of Next Generation HLA allele Sequencing (NGS) in over 1,000 patient samples

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: BACKGROUND: Precision in allelic definition is critical for accurate epitope imputation within a national eplet-matching program. The detailed QC performance program reported here confirms that Next-Generation Sequencing (NGS) can generate high-resolution genotypes with a minimal and predictable error rate. METHODS: Genotyping by Holotype HLA NGS Assay v3 (Omixon, Budapest) for all 11 classical HLA genes (A, B, C, DRB1/3/4/5, DQA1/B1, DPA1/B1) was performed. Confirmatory testing for QC purposes was performed using LABType reverse sequence-specific oligonucleotides or MicroSSP sequence-specific primer technologies (One Lambda, California) to verify accuracy. RESULTS: 1054 samples were sequenced in 48 runs, averaging at 22 samples/run. Guided by our prior QC program, confirmatory testing of 1 or more genes was performed in 86 samples (8.2%) comprising a total of 94 retested loci (Image1). Of the loci retested, 46 tests (48.9%) arose from a queried drop-out, and 10 verified a true drop-out: an allele present but not detected by NGS (Image2). These were DQB1*03:01, DQB1*03:02, and DRB4*01:01, and dropped out only when the gene was heterozygous for another allele; likely due to PCR amplification bias. 24.4% of retested loci were due to questionable QC metrics, such as low coverage, which was commonly seen in intron 2 of DRB1/3 which is rich in homopolymers. As a troubleshooting measure, increasing the number of reads used in analysis improved some low coverage, low read count, and phasing issue warnings. In comparison to the previous version of the kit (v2) there have been significant decreases in confirmatory testing. Dropout testing decreased to 4.2%, QC metric testing to 2.0%, and the detection of true dropouts to 0.9%. CONCLUSION: Advances in NGS chemistry enabled an important increase in precision and reliability with a reduction in drop-outs and improvement in QC metrics. NGS is a simple, reliable, and preferred technology to produce high-resolution HLA genotypes for eplet-matching.

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/44_AbstractImage2_0602095524.pdf

DraftModeStatus: 0

ID: 45
PROGNOSTIC IMPLICATIONS OF HEMOGLOBIN IN ADULT AMBULATORY HEART FAILURE PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND Anemia is a common manifestation of heart failure (HF), and hemoglobin levels have been previously implicated with greater risk of mortality in the growing HF population. This systematic review and meta-analysis aims to investigate the prognostic ability of hemoglobin in predicting all-cause mortality in adult ambulatory HF patients. METHODS In collaboration with an experienced librarian, a comprehensive search was conducted utilizing Embase, Medline, Cochrane, CINAHL and Pubmed through October 2018 to search for studies evaluating the association between hemoglobin and all-cause mortality in ambulatory HF patients using multivariable analysis. Two independent reviewers completed screening, data extraction and quality appraisal. Study quality was assessed in duplicates with Quality of Prognostic Studies. A random-effects model was employed to meta-analyze study results. Subgroup analyses were decided a priori to investigate sources of heterogeneity. RESULTS From a total of 241, 737 citations, 59 studies were included in the final analysis. Forty-one studies evaluated serum hemoglobin as a continuous predictor; a 1g/dL decrease in hemoglobin was associated with 10% increase in mortality (HR1.10, 95%CI 1.08-1.12, I2 = 86%). Eighteen studies evaluated hemoglobin as a categorical predictor defined by < 12g/dL in women and < 13g/dL in men. Hemoglobin levels below the cut-off were associated with 44% increase in mortality (HR1.44, 95%CI 1.30-1.60, I2 = 57%). This effect was accentuated in studies including older population and higher proportion of females. Age and sex accounted for 63.85% of heterogeneity (p=0.0312). Ischemic cardiomyopathy, renal function, ejection fraction, diabetes, New York Heart Association, and risk of bias did not explain the heterogeneity across studies. CONCLUSION In this study, decreased hemoglobin levels are associated with higher risk of mortality in adult ambulatory HF patients, with higher impact in older and female patients. Predictors of mortality in HF are critical to guide treatment plans and should be evaluated in clinical assessments.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/45_AbstractImage1_0602114043.pdf

Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/45_AbstractImage2_0602114043.pdf

DraftModeStatus: 0

ID: 46
Evaluating multiple living kidney donor candidates simultaneously or sequentially: a cost-effectiveness analysis

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Multiple living donor candidates often come forward to donate a kidney to the same recipient. To manage resources and to avoid unnecessary evaluations, some living donor programs choose to evaluate only one candidate at a time. Methods: We modeled 2 to 4 candidates coming forward at the same time to be evaluated as kidney donors for one recipient, assuming that at least one candidate would donate if they completed their evaluation. We modeled competing events to living donor transplantation, including recipient death or receipt of a deceased-donor kidney transplant (some patients remain on the deceased donor waiting despite having a living donor candidate). We examined scenarios when the intended recipient was receiving maintenance dialysis at the start of donor candidate evaluation or potentially pre-emptive. We used a Markov model with a lifetime horizon from the perspective of the primary payer. Results: Under all scenarios, evaluating multiple candidates simultaneously dominated sequential evaluations (greater healthcare cost savings and higher recipient quality-adjusted life years gained). This was due to a shorter total period to evaluate donor candidates prior to transplantation, translating into more living kidney donor transplants, less time on dialysis, and more pre-emptive transplants. Results were most sensitive to the living donor evaluation time, the cost of dialysis, the cost savings due to transplantation, and the probability of starting dialysis (if the recipient was potentially pre-emptive at the outset). Conclusion: Living donor programs should consider evaluating multiple candidates simultaneously when they come forward for the same recipient at the same time.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/46_AbstractImage1_0520092436.pdf

DraftModeStatus: 0

ID: 47
Understanding, measuring, and defining the living donor evaluation process for quality improvement: a Delphi study

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: The living kidney donor evaluation process is not donor-centric. It can exceed 10 months, which places undue stress on donor candidates and their intended recipients. During this time, unintended adverse consequences can arise, including recipient illness or death. To improve the efficiency of the living donor evaluation process across the country, we need to establish key metrics for quality improvement. Methods: We conducted a modified-Delphi study, engaging patients, healthcare professionals, and healthcare administrators (stakeholders) across Canada. Using the literature and conversations with stakeholders, we identified a list of potential quality indicators that can be used to measure the efficiency of the living kidney donor evaluation process. Participants were asked to rate the importance of 12 definitions, 13 process indicators, and 10 outcome indicators on a 9-point Likert scale through an online survey (REDCap). Agreement was measured using the RAND methodology. Further clarifications were discussed at an in-person meeting in May 2019. Results: A total 129 participants were invited to participate in the survey. Among these, 77 (60%) responded. Most participants identified as white/Caucasian (80%) and female (66%). Participants resided or received care across the country, with representation from every province. About half (N=42, 55%) identified as patients, the majority of whom were living donors (79%). Thirty-six percent of participants identified as healthcare professionals (N=27). We achieved agreement on most definitions and quality indicators, although analysis is on-going. Despite agreement on several indicators, participants provided comments that were useful to clarify, re-word, or add new indicators. Four additional process indicators were identified. Discussion: To promote buy-in across transplant programs, it is essential that we achieve consensus on quality indicators that can be used to compare the performance across the country. Next steps will focus on presenting the final list of indicators and discuss their feasibility (e.g. additional data collection).

DraftModeStatus: 0

ID: 49
Human Leukocyte Antigen (HLA) Eplet frequencies in Sensitized Waitlisted Renal Transplant Patients

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction HLA eplets (polymorphic amino acid residues on HLA molecules) determine the specificity of HLA antibodies that form after non-self HLA exposure. Donor-recipient eplet mismatches in solid organ transplant contribute to adverse graft outcomes. Not all eplets however may be equally immunogenic. In this exploratory study, in waitlisted pre-sensitized kidney transplant patients, we sought to examine the frequency of eplets driving observed HLA antibody patterns, and determine their immunogenicity. Methods HLA matchmaker was used to determine the most likely eplets driving observed antibody patterns. An MFI cutoff of 500 was used for inclusion in analysis. Patients were excluded if typing information was not complete (n=41) . Eplet frequency was defined as the number of patients with a given epitope identified, divided by the total number of patients. To calculate the frequency of antigens carrying any given eplet in the population we used the Canadian cPRA calculator (https://ctr2.transplantregistry.ca/otd-cpra-client/ctr2.jsp. Immunogenicity score was defined as eplet frequency divided by the sum of frequency of antigens carrying the eplet . Results 438 patients were included in the cohort (228 male (52%)). Mean cPRA level was 63% (SD 37%) . We identified 155 unique eplets contributing to antibody formation, from which immunogenicity scores were calculated. The five most immunogenic class 1 and class 2 eplets are shown below Eplet Immunogenicity Score Corresponding HLA antigens Eplet frequency in antibody formation Eplet frequency in general population 62GRN 1.853 B57, B58 0.171 0.092 17RS 1.592 A30 0.087 0.055 76ESI 1.319 A25, A32 0.119 0.090 71SA 1.211 B57, B58, B15 0.112 0.092 62LQ 1.191 A29, A43 0.096 0.081 75S3 3.998 DQA*2 0.980 0.245 55RL3 0.726 DQB1*4 0.053 0.0723 16Y 0.638 DRB1*08 DRB1*12 0.075 0.118 57DE 0.634 DRB1*11 0.114 0.180 25Q3 0.475 DRB1*7 0.116 0.245 Conclusions These ten eplets appeared to drive antibodies more commonly than other class 1 and class 2 eplets. These represent candidates for further study regarding potential biological reasons for immunogenicity, and any differential impact of mismatch at these eplets on transplant outcome.

DraftModeStatus: 0

ID: 50
Mitochondrial Permeability Regulates Heart Graft Ischemia-Reperfusion Injury and Allograft Rejection

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND: The clinical relevance of ischemia-reperfusion injury (IRI) in the context of organ transplantation is well-established. IRI is associated with various forms of programmed cell death (PCD), of which necroptosis is particularly significant. Necroptosis is an inflammatory form of PCD that promotes alloimmunity and adversely affects allograft viability and function. We have recently shown the role of cyclophilin D (CypD), a critical mediator of mitochondrial permeability transition pore (mPTP) formation, in microvascular endothelial cell (MVEC) necroptosis. In this study, we investigate the role of CypD in mitigating IRI-induced MVEC necroptosis and the subsequent alloimmune response in a clinically relevant scenario of heart transplantation. METHODS: To model ischemic insult in vitro, MVECs were exposed to hypoxia in glucose-free medium. To model the reperfusion event, MVECs were then transferred to a normoxic incubator in cell culture medium. Cell death was monitored by live-cell imaging and flow cytometry. For in vivo studies, C57BL/6 heart grafts were subjected to cold ischemia storage before transplantation into BALB/c mice. Histopathological grading of IRI and allograft rejection was done by a pathologist. RESULTS: Our data indicate that inhibition of caspases during hypoxia decreases apoptosis but increases necroptosis and that inhibition of CypD attenuates hypoxia-induced necroptosis. Interestingly, apoptosis-inducing factor (AIF) silencing also attenuates hypoxia-induced necroptosis. Our immunocytochemistry studies indicate that mPTP formation facilitates AIF translocation following IRI. Our in vivo studies confirm that CypD deficiency in ischemia-treated donor heart grafts mitigates IRI and allograft rejection (n=8, p=0.008). CONCLUSION: Our studies indicate that regulation of mitochondrial permeability via CypD inhibition following transplantation substantially attenuates necroptosis and the subsequent alloimmune response. Our data also suggest that AIF may be the downstream effector molecule that executes IRI induced necroptosis. As such, targeting mitochondrial permeability may be a plausible approach in formulating therapeutic strategies aimed at reducing IRI induced PCD associated with organ transplantation.

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/50_AbstractImage2_0520102543.pdf

DraftModeStatus: 0

ID: 51
Assessment of predictive biomarkers associated with primary graft dysfunction in lung transplants

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Lung transplantation is the only therapeutic option for patients with a terminal lung condition associated with cystic fibrosis (CF), idiopathic pulmonary fibrosis (PF/IPF), chronic obstructive pulmonary disease (COPD), arterial pulmonary hypertension (APH) or emphysema (EMP). Unfortunately, survival rates at 5-yrs after transplantation (65%) remains too low. Primary graft dysfunction (PGD) is the first cause of death in the perioperative period and is associated with acute respiratory distress syndrome (ARDS), higher risk of lung infection, chronic rejection and lower survival rates. We hypothesized that alveolar epithelial dysfunction in the donor graft and then in the recipient is a critical component of PGD pathophysiology. Our goal is to identify novel biomarkers associated with epithelial dysfunction in the donor's graft and PGD development in the recipient. Methods: We collected the clinical data from 100 donors and their recipients as well as blood, bronchoalveolar lavages (BAL) and lung tissues from the donors and the recipients at different time points, i.e. before, during and after lung transplant (in the perioperative period at the ICU and follow-up visits at the transplantion clinic). The levels of inflammatory, alveolar damage/integrity and functionality markers were then determined. Results: Among the recruited 100 lung transplants (including 53 CF, 25 PF/IPF, 9 COPD, 5 APH, 5 EMP), 39% developed a PGD (score 2 or 3). We noted elevated inflammatory cytokine levels in the BAL post-graft reperfusion in lung recipients with PGD. Similarly, histological analysis of lung biopsies from the donor graft showed alveolar inflammatory infiltration and epithelial damage. Immunofluorescence staining on these lung sections as well as isolated alveolar cells also revealed reduced expression of integrity (ZO-1 protein) and functionality (ENaC channel) markers. Conclusion: This study provides novel insights on epithelial dysfunction within donor's graft associated with PGD development and pave the way for the identification of novel biomarkers.

DraftModeStatus: 0

ID: 52
Implementation of a Web-based tailored nursing intervention in a hospital setting to support optimal medication adherence among kidney transplant patients: stakeholders' consultation and mobilisation

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Transplant-TAVIE is a Web-based tailored virtual nursing intervention developed to promote adherence to immunosuppressive medication and to support selfmanagement among kidney transplant recipients (KTRs). Following the evaluation of the intervention's acceptability, feasibility and preliminary efficacy, the aim is to implement Transplant-TAVIE in a real healthcare setting—the kidney transplant clinic at the CHUM—and to evaluate the outcomes. Consultation sessions were held to take into consideration stakeholders' needs and expertise. Methods: Three consultation sessions, based on a co-construction method and a design thinking approach, were conducted to identify the intervention's strengths and weaknesses, the barriers and facilitators, and the adoption and implementation strategies. In total, 12 participants attended the sessions; these individuals were representative of the stakeholders involved in the project (patients, nurses, physicians, psychologists, social workers, pharmacists and administrators). The SWOT analysis technique was used to structure the discussions. Two research assistants took notes during the sessions. Results: The consultation sessions provided essential information about participants' particular clinical context and helped to develop an implantation strategy that takes into account the reality of the transplant clinic. They identified new KTRs and young KTRs as target populations. Based on the needs of the stakeholders, our findings stressed the importance of having a communication plan, providing training to the healthcare professionals involved, and engaging patient partners before and during the implementation process to support the implementation strategies. Conclusion: Transplant-TAVIE is a personalized and accessible aid to help KTRs manage their immunosuppressive medication and associated adverse effects. The results of our consultation will allow us to implement our intervention in an appropriate manner for the different stakeholders. The implementation study will document the indicators for implementing, anchoring and integrating this new intervention as well as indicators of use and effectiveness among KTRs.

DraftModeStatus: 0

ID: 53
Quebec's healthcare professionals' perspectives on ethical issues related to organ donation after medical assistance in dying.

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: In Quebec, medical assistance in dying (MAID), in the form of euthanasia by physician-administered injection, has been available since December 2015. This change in the end-of-life context has given rise to the possibility that patients requesting MAID could also donate organs through a controlled donation after cardiocirculatory death (cDCD) protocol. In 2018, 15 persons donated their organs after MAID in Quebec, accounting for almost 10% of all donors. This new type of donation raises new ethical questions. The objective of this study is to gather healthcare professionals' (HCPs) perspectives on ethical issues related to MAID and organ donation. Methods: Twenty-two HCPs involved in organ donation or MAID (nurses, intensivists, MAID provider) in Quebec took part in semi-directed interviews between November 2016 and February 2018, during which they had to comment on clinical vignettes and answer open-ended questions. The content of the interviews was analyzed using thematic content analysis. Results: HCPs who participated in this study supported organ donation after MAID because it is a way to respect the person's autonomy at the end of life. Potential pressures to choose MAID for organ donation, the complex assessment of the motivations for choosing MAID and organ donation, the type of information to provide to potential donors and the public perception of MAID and organ donation were the principal ethical issues indicated by the participants. Although they identified different challenges associated with MAID and organ donation, all but one were willing to participate in situations of MAID and organ donation. Conclusion: This is the first study looking at the HCPs' perspectives on ethical issues related to organ donation and MAID. The results highlighted a knowledge gap regarding the donor's motivation and the decision-making process. Further studies are needed to understand them and develop tools to support potential donors and families.

DraftModeStatus: 0

ID: 54
low rate of preemptive kidney transplantation: A root cause analysis to identify opportunities for improvement

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Background:Preemptive living donor kidney transplantation, has several advantages over transplantation after dialysis initiation including improved patient survival and reduced healthcare costs. The St. Joseph's Healthcare Hamilton transplant program performs approximately 30 living donor kidney transplants each year, however only 20% of are preemptive. When trying to improve complex healthcare problems such as this, an in-depth root cause analysis can be conducted to fully understand program-related barriers. Methods:We conducted a retrospective observational study of random sample of 50 living donor kidney transplants in our program that were performed between January 1, 2017 and September 30, 2018. Root Cause Analysis (RCA) provided methodology for this study. Results: Of the 50 recipients, only 11 (22%) achieved a preemptive transplant. The majority of those who achieved a preemptive transplant were referred with a GFR ≥ 15 (64%). Sixteen recipients (32%) were already on dialysis at the time of referral. Of the remaining 23(46%) who were referred preemptively, Major root causes were identified, 18 (78%) had a GFR less than 15 at the time of referral, 12 (37.5%) had medical issues resulting in delayed clearance for transplant, 9 (28%) participated in the Kidney Paired-Exchange program and 8 (25%) required evaluation of multiple living donors before an eligible donor was found. On further analysis of the durations for assessment milestones, it was found that the median time from recipient referral to clearance was just over 13 months. It was also found that the median time from donor contact to clearance was nearly 8 months. Both of these were longer than ideal. Conclusion: Our analysis demonstrates that the timing of recipient referral is a significant cause of failing to achieve preemptive kidney transplantation. Additional studies with further investigation of referral practices and modality education as well as causes for delays during the assessment process are needed.

DraftModeStatus: 0

ID: 55
An interim analysis of the feasibility and acceptability of a mobile phone application in kidney transplant recipients

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Mobile health (mhealth) apps can improve medication nonadherence. Few studies have reported the uptake of mhealth apps in kidney transplant (KTx) recipients. This interim analysis examines the acceptability and feasibility of using a mHealth app in KTx recipients. Methods: This prospective cohort study included primary KTx recipients over a 7-month period between 2018 and 2019. Patients were excluded if they could not read or speak English, did not own a smartphone, required compliance packing for transplant medications or had previous organ transplants. Patient-reported medication adherence was evaluated using BAASIS and usability of the Medisafe app was evaluated using the System Utility Scale (SUS). Results: 75 patients received kidney transplants during the study period. 39 patients met the inclusion criteria and 27 patients provided consent (recruitment rate = 69% (27/39), Figure 1). The proportion of patients who owned a smartphone was similar to the reported Canadian average (79%). Screen failure due to patient inexperience with smartphone usage for mHealth uptake was an important contributor to our low retention rate (48%). Screen failure patients and patients without a smartphone were similar in age (p=0.79) (Figure 2). Patients that regularly used a smartphone were younger than patients who did not own a smartphone (p=0.0045). Among the 5 patients who discontinued the app during the study period, those who required a change to compliance packaging were older compared to patients who requested to discontinue because they felt comfortable with their medications without app reminders. All patients who completed the SUS found the app to be easy to use. Conclusion: We found age to be a determinant in the uptake of mHealth apps in KTx recipients. This data may assist with sample size estimation for prospective trials involving the implementation of mHealth apps.

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DraftModeStatus: 0

ID: 56
The need for intraoperative mannitol or furosemide: an international survey

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Intraoperative mannitol and furosemide have been used as free radical scavengers and diuretics to ignite early renal allograft function. As the evidence of any efficacy of these agents are limited, we sought to characterize the use of intraoperative diuretics among transplant surgeons. Methods: An anonymous online survey of all Canadian surgeons who perform kidney transplants as well as a select number of U.S. transplant surgeons was performed. Questions were related to the use and indications for mannitol and furosemide. Responses were collected and analyzed as counts and percentage of respondents. Chi-square analysis assessed the relationship of demographic factors and survey responses. Results: The response rate was 50% (n=35). Eighty eight percent of respondents reported performing > 50 transplants/year, with 88% fellowship trained, and 67% currently training fellows. Only 24% believe mannitol reduces delayed graft function, yet 73% routinely give mannitol. Only 12% believe furosemide reduces delayed graft function, yet 53% report its routine use. Of routine diuretic users, 58% of respondents report giving both mannitol and furosemide routinely (33% overall report giving both). The most common rationale for the use of mannitol was to induce diuresis (54%); 37% report using mannitol based on training 'dogma'. A similar rationale for furosemide was observed: 57% use for diuresis, with 23% reporting use based on dogma. There was no relationship between fellowship training, case volume, or teaching status on the use of any agent. Seventy one percent reported the need and interest in participating in a randomized trial evaluating the utility of intraoperative diuretics. Conclusions: Intraoperative diuretics utilization and rationale varies amongst surgeons. A substantial number of surgeons use these medications based on "dogma" alone. A randomized trial is justified to better clarify the role of intraoperative diuretics.

DraftModeStatus: 0

ID: 57
Validation of the PROMIS Preference scoring system (PROPr) in patients on dialysis and kidney transplant recipients (KTR)

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

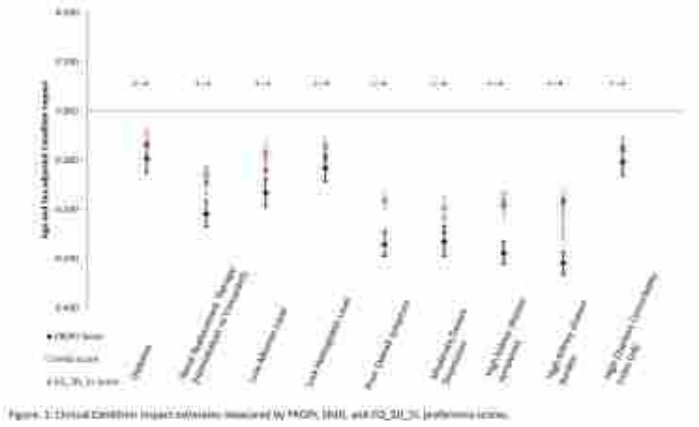
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: PROPr is a preference-based health state summary score within the Patient-Reported-Outcomes Measurement Information System (PROMIS). It could potentially be used in cost-effectiveness analyses. We assessed the validity of PROPr among patients with end stage kidney disease (ESKD) using EQ5D5L and SF6D as "legacy" instruments. Methods: A cross-sectional sample of adults on dialysis and KTR (kidney transplant recipients) completed questionnaires including PROMIS57 (7 domains: anxiety, depression, fatigue, physical-function, sleep-disturbance, pain-interference and ability to participate in social-roles), Patient Health Questionnaire-9, Edmonton Symptom Assessment Scale-revised, Kidney Disease Quality of Life-36 (KDQOL36), and EQ5D5L. SF6D was generated from the SF12 (part of KDQOL36). PROPr is estimated from PROMIS57 domain-scores. PROPr score ranges from -0.022 (all-worst state) to 1.0 (full health). Known-group comparisons were evaluated using age and sex-stratified median scores and calculating "clinical condition impacts", that is the coefficient for a health condition when summary score was regressed on age, gender, and a single health condition. Convergent validity was assessed with Pearson correlation. Results: Mean ([Standard deviation] SD) age of the 318 participants was 57 (17) years, 57% were male and 51% Caucasian. Median ([Interquartile range] IQR) scores were 0.38 (0.22-0.61), 0.71 (0.58-0.86) and 0.85 (0.67-0.91) for PROPr, SF6D and EQ5D5L, respectively. PROPr and SF6D scores were less subject to ceiling-effects compared to EQ5D5L. The age and sex adjusted condition impact was larger for PROPr for all conditions tested compared to the other two scores. Condition impact for PROPr was: kidney transplant recipients (KTR) vs. dialysis (-0.21, P < 0 .001), low vs. high comorbidity (-0.10, P < 0 .001), and low vs. high depression (-0.31, P < 0 .001) (figure. 1). Strong correlations were observed between PROPr and EQ5D5L (rho=0.67) and SF6D (rho=0.74). Conclusions: These results support the validity of PROPr among patients with ESKD. Moreover, PROPr may be more sensitive to differences in health states compared to other preference-based measures.

Abstract Image 1:



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DraftModeStatus: 0

ID: 58
The Transplant Support Physician Model of Deceased Donor Organ Allocation in Ontario

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Since 2010, allocation of deceased donor organs in Ontario has been supported by an on-call group of transplant-support physicians (TSP) advising about donor and organ eligibility such as infection and cancer risk, unique and additive co-morbidities, and logistics. These calls are brief (< 5 minutes) and usually singular. Cases that are not ruled out during these calls then proceed to individual organ offers to the six transplant programs in Ontario. Methods: We reviewed all referrals to the provincial resource center with complete data on TSP involvement for fiscal years 2015-18. Results: During the study period, there were a total of 17,285 donor referrals and 2,399 (14%) of them required a TSP consult. When the TSP was consulted, referred donors were ruled out in 613 (26%) cases. The remaining cases with TSP consults (1,786, 74%) had their organs offered to programs, and 737 (41%) of these had at least one of their organs transplanted. In comparison, for the 14,886 (86%) donor referrals not involving the TSP, 11,372 (76%) were ruled out, while 3,514 (24%) had their organs offered to programs. Of these, 226 (6%) had at least one of their organs transplanted. Conclusion: In summary, the number of donors being referred and offered to programs is increasing annually necessitating a change to the conventional model of calling each program directly with offers. The TSP model active in Ontario provides support in 14% of all donor referrals. A quarter of these can be excluded immediately resulting in improved efficiency in both the allocation system (by avoiding unnecessary calls to programs) and the donation process (by avoiding unnecessary delays). This also results in improved end of life care for the referred donors.

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DraftModeStatus: 0

ID: 59
Effects of a renal nordic walking program on quality of life and fitness in renal patients

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Exercise has been shown to improve symptoms, function, and mental health. Despite the fact that medical guidelines recommend regular physical activity for persons living with renal disease, many people struggle to fit this into their lifestyle. Hospital-affiliated group exercise programs for outpatients can potentially reduce fears and increase exercise self-efficacy. This study investigated the effects of a 3-month supervised Renal Nordic walking (NW) program on the fitness and quality of life of renal outpatients. Thirty participants, aged 45-84 were randomized to NW (n=15) or non-NW (n=15) groups. The NW group was offered 2 supervised NW sessions per week; the non-NW group continued their own activities. No blinding of intervention or outcome assessment was possible. Outcome measurements at baseline and 3-month included weight, handgrip strength (HGS), 30-sec sit-to-stand test, 6-min walk test (6MWT), and Kidney Disease and Quality of Life questionnaire (KDQOL-36). Daily steps were recorded using Fitbit Flex2 tracker during the 3-month study. Using the intention-to-treat principle, changes in outcomes for each participant from baseline to 3-months were calculated and median changes between NW and non-NW group were tested with a Brown-Mood median test. Participants included renal transplant [n=10], pre-dialysis [n=14], hemodialysis [n=3], and peritoneal dialysis [n=3]. Two participants in the non-NW group were lost to follow-up and missing data was minimal. The NW group appeared less healthy compared to the non-NW group at baseline. However, the NW group had greater improvements in KDQOL-36 (Effect of kidney disease; p=0.021), 6MWT distance (41.5m), and HGS (1.1kg) at 3-month. A 14.0 –30.5m improvement in 6MWT is considered important, which was achieved in the NW group. Although a larger number of participants are needed to confirm these findings more confidently, these encouraging results indicate that a group-based supervised Renal NW program may provide benefits to renal patients as part of their clinical care.

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/59_AbstractImage2_0529012521.pdf

DraftModeStatus: 0

ID: 60
Changes in kidney function following live donor nephrectomy

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

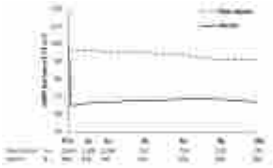
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Better understanding the decline in kidney function after live donor nephrectomy and how this differs by donor characteristics can inform counselling, selection, and follow-up care. Methods: We conducted a retrospective matched cohort study of living kidney donors in Alberta, Canada between 2002 and 2016 using linked healthcare administrative databases. We matched 604 donors to 2,414 healthy non-donors from the general population based on age, sex, year of cohort entry, urban residence, and estimated glomerular filtration rate (eGFR) before cohort entry (nephrectomy date for donors and randomly assigned date for non-donors). The primary outcome was rate of eGFR change over time (median follow-up 7 years, maximum 15 years). Results: The median age was 43 years, 64% were women, and the baseline (predonation) eGFR was 100 mL/min/1.73 m2. Overall, from 6 weeks onwards, the eGFR increased by +0.35 mL/min/1.73 m2 per year (95% CI +0.21 to +0.48) in donors and decreased by -0.85 mL/min/1.73 m2 per year (95% CI -0.94 to -0.75) in non-donors (p < 0 .001). The change in eGFR between 6 weeks to 2 years, 2 to 5 years, and ≥5 years onwards in donors was +1.06, +0.64, and -0.06 mL/min/1.73 m2 per year, respectively. The change in eGFR over time in donors varied by sex, percent decline in eGFR within the first 6 weeks, and eGFR category at 1 year, but not by age category at donation, predonation hypertension, or predonation eGFR category. Conclusion: The function in the remaining kidney of a living donor initially increases by 1 mL/min/1.73 m2 per year due to hyperfiltration; however, this begins to plateau by 5 years postdonation. In contrast, non-donors experience a steady age-related decline of ~1 mL/min/1.73 m2 per year.

Abstract Image 1:



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DraftModeStatus: 0

ID: 61
Feelings and perceptions of the Travelling Donor

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction Since it's inception, the Kidney Paired Donation program (KPD) has helped expand the living donor pool. The Canadian KPD has utilized a travelling donor model (TDM), but is now exploring a transition to a Kidney Shipment Model (KSM). A hybrid system using both these models could lead to an improvement in donation numbers. To help with this transition we set out to examine feelings and perceptions of the traveling donor with the goal to optimize the donor experience and to facilitate a smooth transition to a hybrid model. Methods Following REB approval, an anonymous telephone survey was conducted to all KPD donors that our program was involved in their workup. Questions were open and close ended, including an agreement score based on a five-point Likert scale. Questions focused on the donor experience during their work-up, during travel, and then post-operatively. Each interviewee was then asked to list and rank the main stressors during the entire donation experience. Results The majority of donors did not perceive travelling to donate as a pitfall of the donation process(72%). However, some travel related factors were seen as drawbacks to the Canadian KPD program, such as lack of complete reimbursement(71%), and the stress of travel expenses(19%). Time to complete donation workup was also a common concern amongst donors(31%), although the vast majority(96%) of donors surveyed were pleased with the team who performed their initial work-up. All donors surveyed reported overall satisfaction with the donation process and would recommend it to others. One third of respondents stated they would have chosen KSM if given the option. Conclusion The results of this study underline numerous important barriers inherent to the TDM model as they are perceived by kidney donors. Identifying these barriers is the first step to improving the overall donor experience with potential benefits for the entire KPD program.

Abstract Image 1:

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Abstract Image 2:

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Abstract Image 3:

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DraftModeStatus: 0

ID: 62
Highly sensitized kidney transplant patients T cells display distinct TCR repertoires

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Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Sensitization to HLA antigens limits patient's access to renal transplantation and causes higher risk of acute rejection and graft loss. T-cell mediators, B-cells and donor-specific antibodies play critical role in allograft rejection and injury. T-cell receptor (TCR) signaling is essential for activation and function of T-cell and the structural features of TCR are critical for alloantigen recognition and response. Here we sought to characterize TCR repertoire in highly sensitized patients (HSP) and non-sensitized patients (NSP). Methods: CD4+ cells from HSP and NSP (n=4 each) were used for analysis of baseline TCR repertoire. One-way MLR was performed by culturing CFSE labeled PBMC with irradiated antigen presenting cells carrying alloreactive HLA antigens for 14 days and alloantigen reactive CD4+ cells (CFSElow) were collected. 5'RACE multiplex-PCR amplification and high-throughput sequencing were performed to profile TCR repertoires from both unstimulated and alloreactive CD4+ cells. Results: TCR repertoires of CD4+ cells showed more clonotype similarity amongst HSP than NSP. Stimulation with alloantigen leads to expansion of several unique and shared alloreactive TCR clones in both HSP and NSP and they exhibited similar clonality, diversity and similarity. However, the total frequency of shared alloreactive TCR clones was higher in the HSP than those of NSP. The complementarity determining region-3 of TCR from both unstimulated and stimulated (CFSElo) CD4+ cells in HSP display a biased usage of V/J genes and significantly different amino acid physiochemical properties including amino-acid length, charge and polarity. These features determine the antigen binding specificity and affinity of TCR suggesting distinct TCR repertoire in HSP. Conclusion: Here, we characterized the unstimulated and alloantigen reactive TCR repertoires in HSP, which are distinguishable from with NSP. These results support further exploration of TCR repertoire to develop tools to predict antigen specificity of TCR and target alloreactive T-cells.

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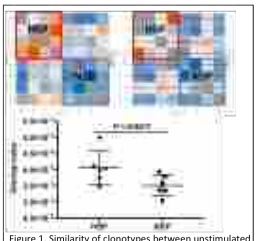

Figure 1. Similarity of clonotypes between unstimulated CD4+ cells of HSP and NSP using Mann-Whitney test.

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Abstract Image 2:

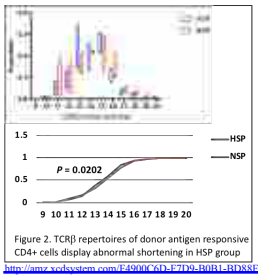

Figure 2. TCRβ repertoires of donor antigen responsive CD4+ cells display abnormal shortening in HSP group

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DraftModeStatus: 0

ID: 63
Pretransplant TNFR2 expressing Tregs as important predictors of renal transplant outcomes

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Few scoring tools like kidney donor risk index (KDRI) exist that rely only on pretransplant metrics and are used during kidney evaluation, but have poor prediction accuracy. Novel pretransplant biomarkers are required to predict recipients at risk of graft dysfunction that may allow optimal donor organ allocation. We had shown that pretransplant recipient TNFR2+Tregs are valuable as an immune marker for delayed graft function (DGF) and acute kidney injury (AKI). Here, we used multiple donor and recipient metrics along with pretransplant TNFR2+Tregs to develop prediction models for various early and late renal transplant outcomes. Methods: A cohort of 76 deceased donor kidney transplant recipients were prospectively followed for outcomes including DGF (n=18; recipients requiring dialysis within 7 days post-transplantation), slow graft function (SGF; n=34; recipients with a decrease in 24-hr serum creatinine by less than 20%) , AKI (DGF/SGF, n=52), biopsy proven acute rejection within 6 months (AR, n=12), rejection within 5yrs (n=19) and graft loss within 5yrs (n=8) post-transplantation. All recipients received ATG, Campath or Daclizumab induction and tacrolimus-based maintenance immunosuppression regimen. Pretransplant CD4+CD127lo/-TNFR2+Tregs were measured by flow cytometry. The recipient, donor and organ procurement characteristics were collected prospectively. Logistic regression and receiver operating characteristic curve analyses were performed to assess the accuracy of predictive models. Results: Recipients with higher TNFR2+Tregs have better graft function. Multiple donor and recipient variables likes KDRI, cold ischemic time, sensitization, T-effector cells, T-helper cells, along with CD4+CD127lo/-TNFR2+Treg cells were utilized to create logistic regression models to predict AKI (AUC=.87), BPAR (AUC=.83), rejection-5yrs (AUC=.73) and graft loss-5yrs (AUC=.86) suggesting importance of pretransplant TNFR2+ Tregs for predicting transplant outcomes. Conclusions: Recipient's immune status as identified by % functional Tregs (TNFR2+) is useful to more accurately predict both short- and long-term graft outcomes. This concept needs to be validated in a larger multi-center prospective study.

Abstract Image 1:

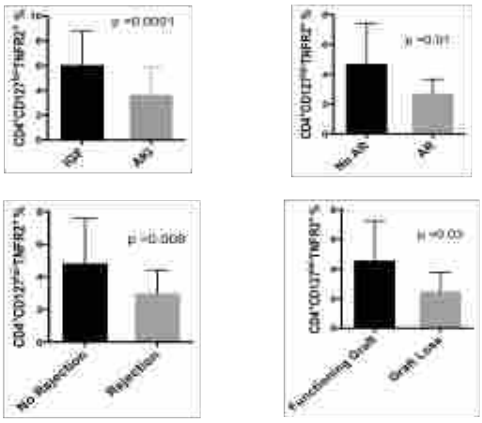

Figure 1. Patients with low circulating TNFR+ Treg have poor transplant outcomes A) AKI; B) AR-6 months; C) Rejection-5 years; D) Graft Loss- 5years.

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Abstract Image 2:

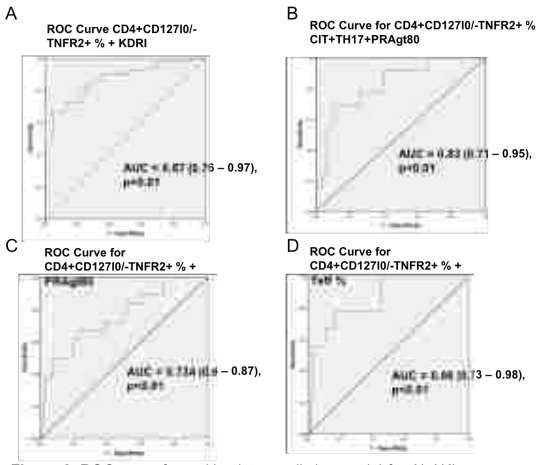

Figure 2. ROC curve for multivariate prediction model for A) AKI and B) AR-6 months C) Rejection -5years and D) Graft-Loss 5years.

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DraftModeStatus: 0

ID: 64
Cell-free DNA release during programmed cell death in kidney ischemia reperfusion injury

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Transplantation is invariably associated with acute allograft injury caused by ischemia reperfusion injury (IRI). This injury causes cells of the allograft to undergo various forms of programmed cell death including apoptosis and necroptosis. During programmed cell death, immunogenic molecules are released from cells, one of which is cell-free DNA (cfDNA). We hypothesize that cfDNA is released by microvascular endothelial cells (MVECs) during programmed cell death of IRI and that cfDNA acts as both a biomarker for cellular injury as well as a biologically active molecule capable of amplifying inflammation and organ injury. Methods: MVECs were subjected to various reagents to induce necroptosis and apoptosis in vitro followed by cfDNA isolation and quantification. A mouse model was used to characterize cfDNA release during IRI. NK cells were subjected to cfDNA in order to determine its biological activity. Results: Our results indicate that cfDNA is released by MVECs under both apoptotic and necroptotic conditions in vitro, as well as during IRI in an in vivo mouse model. We have also shown that cfDNA release is ameliorated by blocking necroptosis in vivo with the use of RIPK3-/-mice that are incapable of undergoing necroptosis. Lastly, we have shown that cfDNA is capable of activating immune cells, showing that NK cell activation markers are upregulated when purified NK cells are subjected to cfDNA in vitro. Conclusion: Our results indicate that cfDNA is a potential biomarker of allograft injury in a renal transplant setting. Donor-derived cfDNA from blood or urine may give rise to novel non-invasive tests to diagnose graft damage. cfDNA also appears to exacerbate inflammation by activating immune cells to produce pro-inflammatory cytokines which further escalates inflammation. It may be prudent to inhibit the release of cfDNA in a transplant scenario, a goal our lab is currently working towards.

DraftModeStatus: 0

ID: 65
The Epidemiology of Early Deep Vein Thrombosis in Kidney Transplant Recipients

Member of: CST

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Kidney transplant recipients (KTR) may be at increased risk for deep vein thrombosis following transplantation and other hospitalizations. Existing reports show a 4.6 to 12.5% incidence in KTR within 1-year of transplant. Since vascular complications such as DVT may decrease patient and graft survival, we investigated the incidence, risk factors, treatments, and outcomes of early DVT among KTR. Methods: A retrospective single-centre cohort study was conducted among adult KTR from January 1, 2005 to December 31, 2016, with follow-up until December 31, 2017. DVT within 3 months post-transplant (early DVT) was diagnosed using appropriate imaging studies (doppler ultrasound, CT, or venogram). Time-to-DVT was assessed using the Kaplan-Meier method. Cox proportional hazard and linear regression models were used to analyze risk factors and outcomes (graft failure, death, hospital readmission) of DVT. Results: There were 71 early DVT events among 1667 KTR, with a cumulative incidence of 4.3% at 3-months post-transplant. Most DVT events were located in the lower limbs and neck/chest (n=20 each). Fifty-three (74.7%) DVTs were only treated medically, 3 (4.23%) only procedurally, and 11 (15.5%) not treated. Recipients of White race (HR 1.84 [95%CI:1.08,3.12]), or expanded criteria donors (HR 2.13 [95%CI:1.05,4.32]) had a higher risk for early DVT. Peri-transplant DVT prophylaxis was not associated with early DVT (p=0.41). Early DVT was not associated with reduced graft function (p=0.39), death (p=0.72), or first hospital readmission (p=0.20) but the risk for graft failure was elevated (HR 2.06 [95%CI:0.97,4.33]). Twelve (16.9%) and 11 (15.5%) patients then developed a second DVT and a pulmonary embolism within 1-year post-transplant, respectively. Conclusion: The incidence of early DVT is comparable to existing literature. Risk factors included White race and expanded criteria donors. DVT was not clearly associated with patient or graft survival. The impact of DVT and other VTE on patient-reported outcomes require further study.

DraftModeStatus: 0

ID: 66
Investigation of the incidence of subclinical rejection from surveillance biopsy findings in kidney transplant recipients with persistent delayed graft function

Member of: CST

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Current standard of care for persistent delayed graft function (DGF) in kidney transplant recipients (KTR) is a surveillance biopsy at day 7-10 post-transplant to detect subclinical rejection (SCR), based on historic incidences of 20-30% in this population. Whether modern incidence of SCR reflects the need for surveillance biopsies remains unclear. Study Objective: To determine recent rates of SCR from surveillance biopsies of persistent DGF patients given anti-thymocyte globulin (ATG) induction and donor-specific antibody (DSA) negative allocation at our center. Methodology: Single-center retrospective cohort study of adult KTR with persistent DGF who received a deceased donor transplant from Feb 1st, 2014 to Dec 31st, 2018. Persistent DGF is defined as the continuation of dialysis at time of biopsy or < 30% decrease in serum creatinine from last hemodialysis session. Patients without biopsy within 2 weeks post-transplantation were excluded. Descriptive recipient and donor characteristics were examined. Proportions of patients with acute rejection on surveillance biopsy among ATG vs. basiliximab-induced patients were compared using the Fisher's Exact test. Results Forty-four patients met the criteria, majority being male (63.6%), non-white (70.4%), median age of 52.5 and donation after cardiac death recipients (84.1%). Patients received induction with either ATG (77.3%) or basiliximab (22.7%) and triple maintenance immunosuppression. Biopsy findings showed 38 cases of acute tubular necrosis (86.5%), and 2 cases each of donor-derived vascular disease (4.5%), acute T-cell mediated rejection (TCMR, 4.5%) and antibody-mediated rejection (ABMR, 4.5%). Among 34 ATG-induced patients, there was 1 case (2.9%) of rejection (ABMR), compared to 3 cases of rejection (2 TCMR and 1 ABMR) among 10 basiliximab-induced patients (30%)(p=0.03). Conclusion: The low incidence of SCR among persistent DGF patients induced with ATG in the current era of DSA-negative allocation of deceased donor kidneys suggests the need to reassess the utility of surveillance biopsies as a standard of care.

DraftModeStatus: 0

ID: 67
Lymphoceles in kidney transplant recipients: Incidence, risk factors, outcomes, and clinical management in the modern era

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Following kidney transplantation, lymphocele development can result in clinically significant morbidity, for both the patient and graft. Lacking prior studies in a representative cohort, we aimed to characterize the incidence, risk factors, outcomes, and clinical management of lymphoceles among modern Canadian renal transplant recipients. Methods: We conducted a single-centre, retrospective cohort study on adults transplanted at our centre between January 1, 2005 and December 31, 2017, excluding patients with simultaneous multi-organ transplants. Incidence, risk factors, and clinical outcomes were determined by the Kaplan-Meier product-limit method, multivariate logistic regression, and Cox regression models, respectively. Results: The cumulative incidence of lymphoceles within one-year post-transplant was 0.35 per 100 person months (CI: 0.28-0.44). Pre-transplant diabetes mellitus (DM) [RR=2.30, CI: (1.20-4.44), P=0.013], laparoscopic donor nephrectomy [RR=2.21, CI: (1.07-4.56), P=0.032], and basiliximab induction therapy [RR=0.46, CI: (0.24-0.89), P=0.021] were significant risk factors for lymphocele development. Recipient ages 55 to 64, polycystic kidney disease, and transplant era 2013 to 2017 were significant only in the univariable logistic model. Contrary to previous studies, recipient BMI was not a significant risk factor. Lymphoceles independently increased the likelihood of hospital readmission (P=0.06), but had no significant effect on the likelihood of total graft failure. Of 78 cases, 62% received either a non-invasive (ultrasound-guided drainage) or invasive (laparoscopic marsupialization) intervention. 35% of cases receiving primary intervention required a second intervention due to reaccumulation within 30 days or complications. Conclusion: Patients affected by DM, undergoing living donor transplantation after laparoscopic donor nephrectomy, and treated with basiliximab induction therapy were at risk for developing lymphoceles associated with increased hospital readmissions, but no other detrimental outcomes. Future studies are required to better delineate the etiology of clinically significant lymphoceles and should consider the efficacy of different interventions in optimizing patient outcomes and refining clinical management to avoid the need for secondary treatments.

DraftModeStatus: 0

ID: 68
The Role of the Renin-Angiotensin System in the Pathophysiology of Chronic Lung Allograft Dysfunction (CLAD) Fibrosis

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background Chronic lung allograft dysfunction (CLAD) remains the leading cause of long-term mortality after lung transplant. Different phenotypes of CLAD exist, all of which result in fibrosis. Angiotensin II (AngII), the main effector of the renin-angiotensin-aldosterone system (RAAS), is involved in fibrogenesis in different organs, most notably in the kidney equivalent of CLAD, Interstitial Fibrosis and Tubular Atrophy (IFTA). We have previously identified AngII-regulated proteins that are elevated in urine and kidneys of patients with IFTA. We hypothesize that RAAS is involved in CLAD pathophysiology and that AngII-regulated proteins will be elevated in Bronchoalveolar Lavage (BAL) and lung tissue of CLAD patients, compared to stable controls. Methods For the measurement of AngII-regulated proteins in BAL, we have developed parallel reaction monitoring (PRM) mass spectrometry-based assays. Two proteotypic peptides of each protein (TSP1, HMOX1, RHOB, BST1, GLNA, LAMB2, LYPA1) were selected. Heavy labeled counterparts of the selected endogenous peptides were spiked in, at known concentrations, to assist with quantification of the endogenous peptides and thus the proteins to which they correspond. We performed immunohistochemistry staining of TSP1 in 2 CLAD lungs and 1 stable control and immunofluorescence staining of AngII receptors 1 and 2 (AGTR1/2) in the lung of 1 CLAD patient. Results Using PRM assays, we detected 2 native peptides of TSP1, BST1, GLNA and LYPA1 protein and one of RHOB in a pool of BAL from controls and patients with CLAD. We constructed calibration curves and determined LOD and LOQ (Figure 1). In our preliminary analysis, AGTR1/2 and TSP1 were identified in characteristic lesions of CLAD (Figures 2-3). Conclusion These preliminary data suggest that RAAS is expressed in CLAD lungs and that AngII-regulated proteins can be measured in BAL. To further these findings, we will quantify AngII-regulated proteins in BAL samples and CLAD lungs from a larger cohort.

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DraftModeStatus: 0

ID: 69
Trends in patient survival among transplant recipients in Canada

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Member of: CST

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background Since organ transplantation became the standard treatment for patients with end-stage organ failure, advances in organ preservation, surgical technique and immunosuppression have contributed to better graft survival and patient outcomes. We present trends in patient survival from the Canadian Organ Replacement Register (CORR), a national registry for patients with end-stage organ failure. Methods We used CORR data collected between 2006 and 2017 from all provinces in Canada excluding Quebec. We calculated yearly estimates of 1-, 5- and 10-year survival (patient and graft, where possible) from all patients with a first kidney, liver, heart or lung transplant from a deceased donor, and investigated the difference in patient survival between patients transplanted from donor after neurological and cardio-circulatory death. Results Patient survival at 1-year post liver transplantation has been stable at approximately 92% between 2006 and 2016. In contrast, 1-year patient survival among heart transplant recipients improved from 87% to 94%, while 1-year survival for lung transplant recipients increased from 85% to 89%. Five-year patient survival for heart transplant recipients was stable (~84%); however, liver and lung transplant 5-year survival increased from 75% to 88% and 56% to 69%, respectively. Amongst kidney transplant recipients, patient survival at 5 years is high (~90%) and kidney graft survival is consistently over 80% at 5 years. Conclusion Patient survival has remained high for kidney and has increased for liver, heart, and lung transplant patients between 2006 and 2017. Although lung transplant patients had the lowest survival rates across all time points, it had the largest absolute increase in survival. Increases in patient survival over time after first transplants are positive trends for these patients. Monitoring and reporting on trends in short- and long-term outcomes after transplantation is valuable and highlights the impact of changes in practice and care of transplant recipients over time.

DraftModeStatus: 0

ID: 70
Liver transplantation for alcohol related liver disease with less than 6 months abstinence: A review of the first year results for the Ontario ALD pilot protocol

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: BACKGROUND In Canada, patients with alcohol-associated liver disease (ALD) require 6 months abstinence prior to liver transplantation (LT). This policy disadvantages acutely ill patients who cannot survive this timeframe. The Ontario ALD Pilot Program was initiated to assess these patients for earlier consideration of LT. We herein present the first year results. METHODS All referrals to the ALD program were triaged using information provided by referring physicians as well as collateral information from a provincial database. Patients were assessed by a team of transplant hepatologists, a nurse practitioner, psychiatrists, an addiction counsellor and a social worker. Random Ethyl Glucuronide (EtG) testing for alcohol was utilized for screening throughout the process. Patients with appropriate indications for transplant, and met the program's criteria, proceeded with the remainder of transplant evaluation. RESULTS From May 2018 to May 2019, we reviewed 224 referrals of which 75% (n= 169) were outpatients with an average MELD score of 21. Eighty-nine patients (40%) did not meet inclusion criteria, including 8 patients (3.6%) who were found to have an initial positive EtG. Fifteen patients (6.6%) were declined for medical fitness. Five patients (2%) clinically improved and were subsequently discharged. Nineteen patients (8%) were listed with a mean NaMELD 31.5 (median 32.5), and ten (4.4%) were transplanted, two of whom expired. All recipients are closely followed through our relapse prevention program and none have relapsed to alcohol use over an average follow-up period of 139.4 days. CONCLUSIONS The first year experience of the ALD Pilot Program demonstrates the complexities of this novel assessment procedure and emphasizes the benefit of the multidisciplinary team approach combined with objective biometric testing. Positive EtG results and the high volume of declined referrals highlight the challenge of addressing addiction in the context of liver disease. Long-term follow-up of post-transplant outcomes are necessary to re-assess the 6-month abstinence policy.

DraftModeStatus: 0

ID: 72
Allograft bioburden reduction as a tissue banking process

Member of: CST

Abstract Type: General Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: BACKGROUND: Bacterial contamination of tissue allografts recovered by tissue banks poses a serious threat to transplant recipients. Although potential donors are carefully screened to mitigate the risk of infectious disease transmission, allograft tissues can become contaminated during recovery. Revisions to Canadian health standards have resulted in a requirement for further quantitative validation of tissue allograft bioburden reduction. The purpose of this study was to quantitatively validate the bioburden reduction of each disinfection process for tissue allografts recovered at a Canadian tissue bank. METHODS: Process characterization was performed for each allograft tissue program including cardiac valves (CV), musculoskeletal (MSK), amniotic membrane (AM), and skin. Each test method utilized in the full bioburden reduction study was validated. Representative allograft samples were inoculated with a cocktail of five challenge organisms identified within the standards (S. aureus, S. pyogenes, E. coli, P. aeruginosa, and C. sporogenes). Allografts were disinfected according to standard operating procedures, followed by recovery of remaining contaminating organisms by ultrasonication and mechanical shaking. The bioburden was quantified using a membrane filtration technique. Blood agar plates were incubated in the appropriate atmosphere and colonies were counted. RESULTS: Test method validation of the recovery method demonstrated the recovery efficiency across all tissue types ranged from 61.89% to 83.33% for aerobic organisms and 47.65% to 88.10% for anaerobic organisms. Bioburden reduction of CV disinfection process was the most stringent (-4.11log ±0.05 aerobic, -4.10log ±0.15 anaerobic) while AM disinfection had the least impactful reduction on bioburden (-0.27log ±0.20 aerobic, -0.57log ±0.39 anaerobic). CONCLUSIONS: Test method validation of the recovery method improved the bioburden reduction validation by demonstrating the recovery efficiency for each tissue type. Although decontamination of tissue allografts differs across tissue programs, this study demonstrates a successful process for validating bioburden reduction within a Canadian tissue bank.

Abstract Image 1:

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DraftModeStatus: 0

ID: 73
Anti-HLA-DR, DP and DQ antibodies leads to different expression of pro- and anti-thrombotic proteins by human endothelial cells.

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

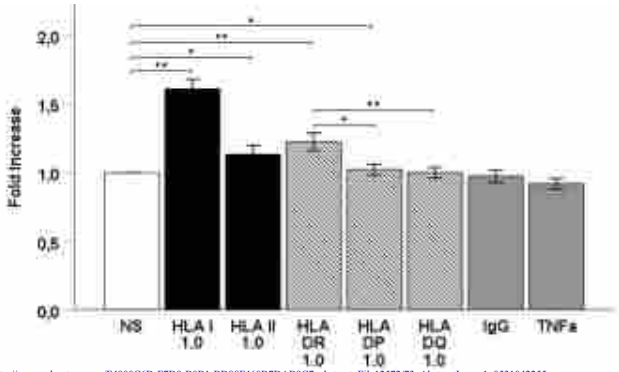
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background. The development of de novo donor-specific antibodies (DSAs), especially against HLA-II antigens, is associated with antibody-mediated rejection and allograft failure. However, mechanistic knowledge about their direct effect on endothelium is lacking. We have previously showed that there is a large variability in the expression of HLA-II antigens between DR, DP, DQ subclasses on endothelial-colony-forming cells (ECFCs, also known as BOECs). Here we hypothesized that in line with the above, stimulation with anti-HLA-DR, DP and DQ antibodies have different effects on endothelial microthrombosis. Methods. We have generated ECFCs from patient's collected PBMCs (n = 14). Cells were stimulated with anti-HLA-I antibody or anti-HLA-II subclass (DR, DP or DQ) antibodies. We measured the endothelial expression of the antithrombotic thrombomodulin versus prothrombotic von Willebrand factor (vWF) using immunofluorescence and ELISA. Results. Anti-HLA-I stimulation increased significantly thrombomodulin membrane expression (Figure 1). Among anti-HLA-II subclasses, anti-HLA-DR and -DP significantly increased membrane thrombomodulin, whereas –DQ was similar to the positive control TNFa (Figure 1). Measurement of soluble thrombomodulin confirmed that low membrane expression with DQ stimulation was not due to increased release in culture supernatant. Regarding vWF, only anti-HLA-DQ led to increased membrane expression of long vWF multimeric strings (absolute increase in long string/cell vs unstimulated cells: DQ, 0.0062; DP, 0.0031; DR; 0.0008). Conclusion. These preliminary results suggest that the endothelial microthrombosis produced by anti-HLA II antibodies varies between subclasses. DQ seems to have a more pro-thrombotic effect by inhibiting thrombomodulin membrane expression and increasing long vWF multimeric strings. These data provide potential mechanisms to explain the difference observed between anti-HLA-II subclasses with regards to transplant glomerulopathy and clinical outcomes.

Abstract Image 1:



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DraftModeStatus: 0

ID: 74
De-novo donor specific antibody development is decreased in patients with thymectomy at an early age

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Member of: CDTRP

Abstract Type: Pediatric Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: De novo donor-specific HLA antibodies (dnDSA) are associated with poor outcomes in pediatric heart transplantation (PHTx). For access to the heart/great vessels, infants undergoing cardiac surgery often need thymectomy, which is known to alter T cell function. Our aim was to investigate the impact of thymectomy on dnDSA production and explore T cell phenotypes in this PHTx population. Methods: Pre-PHTx antibody testing was performed by solid-phase testing/screening; post-PHTx dnDSA were determined by single antigen beads. Persistent dnDSA were defined as detected more than once. Strong dnDSA were defined as MFI>3000. A pilot subset (n=5) was immunophenotyped to explore naïve (CCR7+CD45RA+) vs central memory (CM) (CCR7-CD45RA+) T cell subsets. Results: Patients were transplanted 2005-2017 (n=136); 28 were excluded due to lack of dnDSA data. Average post-PHTx testing follow-up was 4.1 years (3.4 SD). Overall, dnDSA was found in 26% of patients (n=27), persistent dnDSA in 17% (n=18), and strong/persistent dnDSA in 8% (n=9) (Figure 1). Thymectomy status was available for 86 pts, n=47 with known thymectomy date. Thymectomy status alone did not predict dnDSA, but dnDSA production was associated with age at thymectomy (p=0.01); patients with thymectomy at an early age were less likely to develop dnDSA. Sex, ABO compatibility, and age at transplant were not associated with dnDSA (Table 1). Pre-PHtx, higher proportions of naïve CD4 T cells were seen in dnDSA+ compared to dnDSA- patients; CM CD4 T cells were decreased (Figure 2). Conclusion: Results suggest that thymectomy at a young age is associated with decreased risk of post-PHTx dnDSA, possibly due to truncated T cell repertoire. Although the pilot numbers are small, the percentage of naïve and CM T cells may provide some prediction of immune function in these patients. Thymectomy studies are challenging due to lack of surgical documentation; the youngest infants may undergo complete (vs partial) thymectomy, which may also explain these findings.

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DraftModeStatus: 0

ID: 75
The outcome of expanded criteria donor kidney transplant: quality improvement study

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

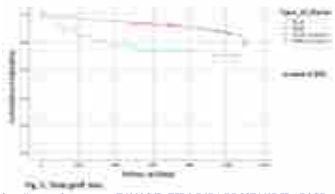
Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction:Donor characteristics that define ECD include age > or = 60 years, or age 50-59 years plus two of the following; CVA as the cause of death, pre-existing hypertension, terminal serum creatinine greater than 132 umol/l (or in Ontario, MDRD eGFR of ≤70 mL/min/1.73 m2). Expanded criteria donor (ECD) kidneys are known to have suboptimal outcomes when compared to standard criteria donor (SCD) kidneys. However, they are widely used to increase the pool of organs offered. Methods:In this quality improvement study, We included all ECD renal transplant recipients in our institution between January 2008 and December 2017. We compared a 3-year patient and graft survival between donation after circulatory death (DCD) and neurological determination of death (NDD). We hypothesized that DCD outcomes would be inferior to NDD outcomes. Results:166 ECD renal transplant recipients, 49 (29.5%) were DCD and 117 (70.5%) were NDD. Mean age was 62 years for DCD recipients and 62.5 years for NDD recipients. 46 (93.3%) DCD recipients and 89 (76%) NDD recipients received thymoglobulin for induction, pvalue 0.008. 30 (61.2%) DCD recipients & 54 (32%) NDD recipients had delayed graft function, pvalue < 0 .001. Mean donor age was 60 years for DCD and 62.5 years for NDD, p=ns. Mean cold ischemia time was 705 minutes for DCD and 790 minutes for NDD, p=ns. Mean terminal creatinine was 62.5 umol/l for DCD & 72.9 umol/l for NDD, pvalue 0.009. 3-year total graft loss was 35 (21.1%): DCD 14 (28.6%), NDD 21(18%), pvalue 0.006. 3-year death-censored graft loss was 23 (13.9%): DCD 11 (22.4%), NDD 12 (10.3%), pvalue < 0 .001. There was no statistically significant difference in all-cause mortality between DCD/ECD & NDD/ECD. Conclusion:It seems that DCD/ECD kidneys have lower graft survival when compared to NDD/ECD kidneys. Time on dialysis, waiting time and panel reactive antibody should be taken into account when offering these organs to patients.

Abstract Image 1:



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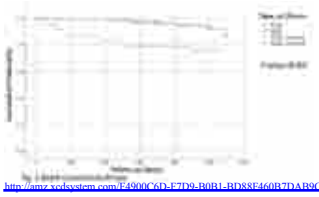

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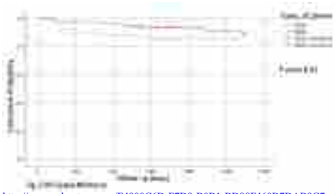

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DraftModeStatus: 0

ID: 76
Efficacy of Trimethoprim-sulfamethoxazole in prevention of urinary tract infection in renal allograft recipients

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction:Urinary tract infection (UTI) commonly occurs after renal transplantation. Post-transplant prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) has been shown to reduce the risk of UTI. The prophylactic effect of TMP-SMX against UTI is not clear while growing number of patients receive this antibiotic to prevent pneumocystis pneumonia (PCP). Method:In this retrospective cohort, all renal transplant patients who received allografts at a single institution from Jan 2011 to December 2013 were included. Patients routinely received TMP-SMX (160 mg/800mg) three times per week for 12 months after transplantation. We determined all episodes of UTI in the first year after transplantation. Results:33/182 recipients (18.13%) developed 57 episodes of UTI (cumulative incidence: 31.3%). Of these, 24.6% were associated with bacteremia (n=14) and 61.4% (n=35) required hospital admission. E. Coli(33.3%) and Klebsiella pneumoniae complex(26.3%) were the most frequent isolates. Although UTI was frequently associated with allograft dysfunction, it did not significantly increase the risk of graft loss (6.1% vs 1.3%, p=0.15) or death (6.1% vs0.7%, p=0.085). Median(range) interval between the first episode of UTI and transplantation was 92 (10-325) days. Age did not significantly increase the risk of UTI (Mean [SD] 52.12 [15.9] years vs 51.44 [12.8] years, p=0.79). 16 out of 61 females (26.2%) vs 17 out of 121 males (14%) developed UTI (p=0.037). 168/182 recipients (92.3%) were on TMP-SMX. 35/57 UTI episodes (61.4%) were with microorganisms resistant to TMP-SMX and half of these (18 episodes, 31.6%) were MDR pathogens. 40 episodes occurred while patients were on TMP-SMX (70.17%). Conclusion:Current guidelines recommend UTI prophylaxis with TMP-SMX at least 6 months after renal transplantation. However, recipients frequently develop UTI with TMP-SMX resistant uropathogens. TMP-SMX (160 /800mg) 3 times/week is not a reliable regimen to prevent UTI even when the causative microorganism is susceptible.

DraftModeStatus: 0

ID: 77
Ongoing efforts to link donor and recipient data in research: the Canada-DONATE Data Link Study

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction Canadian research to improve the medical care of deceased organ donors is challenged by the regionalization of donation and transplant services across provinces, and inconsistent research access to individual transplant recipient data. Objective To support clinical research that will establish best care for deceased organ donors, we endeavored to build a live compendium of provincial and national databases of organ transplant outcome data. Methods We developed a 23-item online survey to assess the content, quality, and accessibility of the databases. In two focus group interviews, donation researchers helped to generate and refine survey items. Three donation researcher/administrators pre-tested the content and completion time. We contacted representatives from 10 provincial and national organizations housing organ recipient data to respond to our online survey, providing telephone support as necessary. Results Each organization responded and six have completed the survey. Five databases record organ recipient vital status (e.g. mortality); four track biochemical and mechanical support data; three track pathology; and two track physiologic function (Table). The period of post-transplant data varies from one to 10 years, with three organizations recording data at regular intervals. Data entry is immediate for provincial organizations, and requires up to one year for national databases. Data validation procedures vary. For clinical research applications, provincial organizations occasionally require direct recipient consent; national databases do not. Estimates of the median time to research access varied from 1-4 months depending on data complexity. Limitations The response rate is 60%. Some items (e.g. time to access) are highly variable, so the compendium is limited to listing the most common result for each organization. Conclusion Completion of this work will result in a living compendium of organ recipient data sources available to Canadian researchers on-line. Next steps will extend this work to individual transplant programs across Canada.

Abstract Image 1:

Table 2: Database Contents and Characteristics

[illegible]	Date Transplant Program Discharge Date	Date of Birth Medical Record Number Health Card Number	No	Biochemical Pathology Mechanical Support Vital Status
[illegible]	Transplant Date Transplant Program Procedural Notes	Date of Birth ODO Number Health Card Number	No	Vital Status
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[illegible]	Date Transplant Program Procedure Notes Date of Discharge	Date of Birth Medical Record Number ODO Number Health Card Number	Yes	[illegible]
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DraftModeStatus: 0

ID: 78
Association between living donor kidney donation transplant (LDKT) readiness and cultural affiliation among patients with end-stage kidney disease

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ethnic minority patients may experience cultural barriers to LDKT, but the extent to which their cultural affiliation is associated with readiness to pursue LDKT is not well understood. Here we assess the association between perceived impact of kidney disease on cultural practices and readiness to pursue LDKT or willingness to share LDKT interest. Methods: A cross-sectional, convenience sample of adult patients with ESKD from dialysis units in Toronto completed the study questionnaire using an electronic data capture system. To assess cultural practices (exposure), patients were asked: “To what extent does your illness or the treatments that you receive cause difficulty with your ability to keep up your cultural traditions”. We also assessed readiness to pursue LDKT and willingness to tell others about interest in LDKT (outcome). Multivariable adjusted multinomial logistic regression was used to assess association between exposure and outcome. Results: A total of 485 participants were recruited (63% male, mean [SD] age 57 [14] years). After adjusting for sociodemographic variables, patients who reported higher impact of kidney disease on practicing their culture were more likely to be at a moderate (RRR = 2.1, CI = 1.0 – 4.6, p = 0.057) or late stage of LDKT readiness (RRR = 3.1, CI = 1.6- 5.9, p < 0.001). These patients were also more likely to be planning to share (RRR = 2.1, CI = 1.1 – 3.9, p= 0.018), or have shared (RRR = 1.7, CI = 0.89 – 3.3, p = 0.10) their interest in LDKT. Conclusion: Patients who perceive a negative impact of kidney disease on practicing their culture were more likely to be at a later stage of LDKT readiness. Pursuing LDKT may allow to return to usual cultural practices for patients who perceive difficulties due to their illness. This aspect could potentially be utilized in culturally competent transplant education.

DraftModeStatus: 0

ID: 79
Assessing Stakeholder Perspectives on Engaging Youth Through A Science Exhibition Regarding Organ Donation and Transplantation

Member of: CST

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Despite educational interventions aimed at improving organ donation awareness among youth, many are not registered organ donors. Innovative initiatives such as an interactive science exhibition (SE) targeting youth may peak interest, dispel misconceptions and promote donation registration. Study Objective: To assess stakeholders' perspectives on utilizing a SE to promote organ donation among Canadian youth. Methodology: Surveys were distributed to healthcare professionals (HCPs), university and high school students and the general public to elicit perspectives on exhibition content and delivery. Survey domains included demographics, knowledge and opinions concerning transplantation, proposed content, and methods of relaying information. Surveys were disseminated through social media platforms and emails targeting HCPs, university clubs and students. HCPs also participated in focus groups and semi-structured interviews to gain additional insight. Results: Investigators received 175 surveys, interviewed 4 HCPs, and held focus groups with 29 participants. Most survey respondents were 16-25 years-old (58%) and interested in attending a transplant SE (83%). While 87% of respondents believed it is important to discuss organ donation, only 45% were registered organ donors. Regarding SE content, respondents were interested in donatable organs and tissues (97%), the transplantation process (89%), life post-transplant (84%) and the organ donor registration process (78%). Respondents believed that content should be delivered via touch displays (70%), 3D anatomical models (68%) and simulations of operations (63%). Results from focus groups and interviews regarding SE content and delivery paralleled those from the survey. Focus group respondents and interviewees also emphasized sharing personal transplant experiences and addressing misconceptions about donor care, registration and organ procurement. Conclusion: This exploratory assessment indicates interest in a transplant SE to promote knowledge and awareness of organ donation. Our findings regarding SE content and presentation will guide the development of exhibit prototypes for user testing in the next phase of this project.

DraftModeStatus: 0

ID: 80
The Use of High Risk Kidney Donors and Long-Term Outcomes: Parameters That Affect Graft Survival

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Kidney transplantation is the treatment of choice in patients with end stage renal disease (ESRD). The introduction of Expanded Criteria Donor (ECD) and Kidney Donor Risk Index (KDRI) may have produced the opposite effect of what was intended. Many centers avoid using kidneys from these donors, fearing unacceptable long-term outcomes. The aim of this study is to assess long-term renal graft survival in a single center with liberal donor and recipient selection criteria and to identify parameters that may influence graft survival. Methods: An analysis of clinical data from 1998 to 2013 was conducted. 686 patients with at least 5 years of follow-up were studied. We excluded patients lost to follow-up (n=69), living donors (n=243) and multi-organ transplants (n=123). Statistical analysis was performed using Cox Regression and Kaplan-Meier survival curve. Results are presented in Table 1 and Figure 1. Results: Of 686 transplant recipients, 274 (39.9%) were from ECD. KDRI was available for 519 patients and identified as low (1.285) with tertile stratification. After censoring for death, factors that increased hazard of graft failure included increased donor and recipient age, increased recipient Body Mass Index (BMI), hypertension as the cause of ESRD, diabetic donors, ECD and increased KDRI (see Table 1). Factors that did not significantly affect graft survival included cold ischemia time and donor creatinine. The median graft survival in this cohort was extrapolated to 16.7 years. Although high KDRI did increase risk of graft failure, as expected, by 255% compared to low KDRI, the estimated graft half life for high and medium KDRI was 12.9 and 18.4 years respectively. Conclusion: Given that even high KDRI kidneys have a graft half-life of almost 13 years, these results suggest there is ample room to expand donor selection without compromising long term outcomes.

Abstract Image 1:

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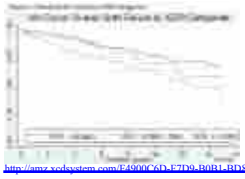

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DraftModeStatus: 0

ID: 81
Predictors of 1-year mortality in liver transplant recipients: a systematic review and meta-analysis.

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Liver transplantation extends life and improves the quality of life for patients with severe liver disease. US registries report a 5-year survival of 81.2% (2016), and highlight several predictors of recipient survival: age, etiology of liver disease, retransplant and MELD score, among others. This study aims to systematically review the predictors of 1-year mortality. Methods: We included studies that applied multivariable regression to identify predictors of 1-year mortality among adult liver recipients. We searched MEDLINE, EMBASE, Cochrane Database of Systematic Reviews and Cochrane CENTRAL. The risk of bias of included studies was assessed by the Quality in Prognostic Studies instrument. We pooled study results using inverse variance method. We rated the overall quality of evidence for each predictor variable using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Results and Conclusion: Among 57 eligible studies, sample sizes ranged from 105 to 53,156 recipients. Outcomes reported were: graft loss (composite outcome including patient death) and mortality. Studies included 589 unique potential predictors related to recipients (380), donors (99) and surgical procedures (110); however, few of these were summarized using meta-analysis. We found the following predictors were significantly associated with mortality: 10-year increase in recipient age (HR 1.14; CI 95% 1.07 – 1.22), 10-unit increase in MELD (HR 1.14; CI 95% 1.07 – 1.22), Donor Risk Index (HR 1.46; CI 95% 1.41 – 1.52), and donor type (DCD vs NDD) (HR 1.65; CI 95% 1.40 – 1.95). Pooling data from 3 studies, we found no effect of recipient BMI, as expressed per 10 unit change (HR 1.00; CI 95% 0.91 – 1.10). Challenges to the conduct of this review included duplicate publications from the same registry, and regression analysis reported with insufficient information (i.e regression model assumptions). This study confirmed some known predictors, and identified new predictors of one-year

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/81_AbstractImage2_0602093015.pdf

DraftModeStatus: 0

ID: 82
Predictors of 1-year graft loss in pancreas transplant recipients: a systematic review and meta-analysis.

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Pancreas transplantation provides metabolic control to selected patients with diabetes mellitus (DM). US registries have reported factors related to graft loss: Type of pancreas transplantation, recipient age, pancreas donor risk index (PDRI). This study aims to systematically summarize all studies reporting predictors of pancreas graft loss. Methods: We included all studies that used multivariable regression to assess predictors of 1-year pancreas graft loss following simultaneous pancreas-kidney (SPK), pancreas-after-kidney (PAK) and pancreas transplantation alone (PTA), in adults. We searched MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews and Cochrane CENTRAL. The risk of bias of each study was assessed using the Quality in Prognostic Studies instrument. We pooled data using inverse variance method. We assessed the quality of evidence for each predictor variable using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Results and Conclusion: Among 19 eligible studies, the number of transplant recipients ranged from 62 to 24,195. Studies investigated 145 unique predictors of graft loss (33 recipient, 32 donor, and 80 procedure-related predictors). Few were summarized in a meta-analysis. We identified 68 statistically significant predictors related to graft loss: 10-year increase in recipient age (HR 1.26; 95%CI 1.11 – 1.44), transplant type (PAK/PTA versus SPK, HR 2.12; 95%CI 1.28 – 3.57) low vs high center volume (HR 1.23; 95%CI 1.09 – 1.36), unit increase of recipient BMI (HR 1.02; 95%CI 1.01 – 1.03), acute rejection (HR 1.70; 95%CI 1.33 – 2.17), 10-year increase in donor age (HR 1.11; 95%CI 1.05 – 1.18) and PDRI (HR 1.52; 95%CI 1.44 – 1.60). Challenges to this study included duplicate publications and regression analysis reported with insufficient information (i.e regression model assumptions). Our results have confirmed known predictors and identified new ones (For example: ultrasound findings as absent or reversed diastolic arterial flow)

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DraftModeStatus: 0

ID: 83
Correlates of fatigue among kidney transplant recipients

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Up to 40% of kidney transplant recipients (KTR) experience significant fatigue. Fatigue has been associated with clinical and psychosocial factors in clinical cohorts, however, those associations have not been explored in KTR. Here we assess correlates of fatigue which may help guide management strategies for fatigue. Methods: A cross-sectional, convenience sample of adult KTRs completed the Patient Reported Outcomes Measurement Information System (PROMIS) fatigue item bank, the Generalized Anxiety Disorder7, the Patient Health Questionnaire9, and the Social Difficulty Inventory on an electronic data capture system. Clinical characteristics were collected from medical records. Multivariable adjusted linear regression models were used to assess the associations between fatigue and potential correlates. Results 274 patients (mean (SD) age 52 (15) years, 56% male and 69% transplanted >3 years before enrollment) were enrolled. The mean (SD) PROMIS fatigue score was 50 (10) and 19% of KTRs were classified as experiencing significant fatigue. Fatigue was correlated with anxiety (Rho=0.56), depressive symptoms (Rho=0.75), and social distress (Rho=0.59; p < 0 .001 for all). Weaker correlations were found with hemoglobin (Rho=–0.26; p < 0 .001) and serum albumin (Rho=–0.13; p=0.03). In separate multivariable adjusted (age, ethnicity, education, marital status, income, comorbidity, estimated glomerular filtration rate and time since kidney transplant) linear regression model, moderate/severe (score of ≥10) anxiety (coeff= 10.63;CI:6.19-15.08), depression (coeff= 14.53;CI:9.94-19.12) and social distress (coeff= 10.81;CI:7.92-13.69) (p < 0 .001 for all) were significantly associated with higher fatigue scores. In addition, female sex (coeff= 3.59; CI:1.01-6.17; p=0.007), lower serum albumin (coeff= -0.50;CI:-0.93- -0.07; p=0.02) and hemoglobin levels (coeff= -0.12;CI:-0.20- -0.05; p=0.001) were also significantly associated with fatigue. Conclusion: Psychosocial factors appear to be more strongly associated with fatigue than clinical variables in KTR. In further studies we will explore if managing those factors could improve fatigue in this patient population.

DraftModeStatus: 0

ID: 85
Successful Desensitization and Kidney Transplantation in the Presence of Donor Specific Anti-Human Leukocyte Antigen Antibodies in Kidney Transplant Recipients

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Sensitization of human leukocyte antigen (HLA) precipitates extensive immunological fences to successful kidney transplantation and henceforth, transplant candidates are frequently demoted to the ever-growing waiting list owing to preformed donor specific antibodies (DSAs). Transplant recipients are at inevitable risk to sustain hyperacute rejection, accelerated acute rejection, early acute antibody-mediated rejection and early graft loss, if DSAs are not sufficiently repressed. Our objective was to evaluate the improvement in kidney function in patients post-desensitization and kidneytransplantation. For the second time in Pakistan, we successfully performed desensitization therapy and HLA-incompatible kidney transplantation in a DSAs positive cohort. Case Presentation: A 23 years old male patient presented with end-stage renal disease (ESRD) secondary to chronic membranoproliferative glomerulonephritis on February 2018. The patient was on hemodialysis for the past 3 months and had a history of hypertension, hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. His blood group was A positive which matched with his sister's blood group. The Luminex technology was used to detect IgG antibodies against the HLA. A significantly high number of DSAs were present against A26 and B51 with median fluorescence intensity (MFI) value of 17692 and 15388, respectively. Lymphocyte crossmatch was performed by complement dependent cytotoxicity (CDC) assay. The CDC crossmatch was positive for both T and Blymphocytes. We then performed following desensitization protocol (Two sessions of Plasmapheresis on day 1 and 2; injection Rituximab on day 2 after Plasmapheresis; no Plasmapheresis on day 3; eight sessions of Plasmapheresis after day 3 and IVIG 100mg/Kg/dose after each session of Plasmapheresis; repeat Luminex technology to confirm if DSAs are present against HLA with MFI values < 2 000 and CDC crossmatch is negative for both T and B lymphocytes; if NO then continue Plasmapheresis sessions with IVIG 100mg/Kg/dose till MFI values are < 2 000 and CDC crossmatch is negative for both T and B lymphocytes or if YESthen proceed for transplantation; and repeat dose of Rituximab post-transplantation) to achieve MFI values < 2 000 and negative CDC crossmatch for both T and B lymphocytes beforeproceeding for kidney transplantation. Our transplant recipient responded well to desensitization protocol with MFI values of 1543 and 989 for A26 and B51, respectively and negative CDC crossmatch for both T and B lymphocytes. The patient was successfully transplanted with kidney on April 2018. On follow up, no remarkable events were noted. Conclusion: We successfully desensitized and transplanted an ESRD patient secondary to chronic membranoproliferative glomerulonephritiswith preformed DSAs against HLA. Our desensitization protocol comprised of multiple Plasmapheresis sessions with simultaneous IVIG and Rituximab, an immunomodulatory drug. The 6 months follow up of recipient did

DraftModeStatus: 0

ID: 86
Kidney function, albuminuria, and the risk of hemorrhage and thrombosis after kidney transplantation

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Compared to the general population, kidney transplant recipients are at increased risk of hemorrhage and thrombosis. Whether this risk is affected by kidney function and albuminuria is unknown. Methods: We conducted a retrospective cohort study using linked healthcare databases to identify adult kidney transplant recipients from 2002--2015 in Alberta, Canada. Estimated glomerular filtration rate (eGFR) and albuminuria measurements at 1--year posttransplant were used to categorize recipients (eGFR: ≥45 vs. ; albuminuria: normal vs. mild--heavy). We determined the association between categories of eGFR and albuminuria and posttransplant hemorrhage and venous thrombosis based on diagnostic and procedural codes. Results: Of 1,284 kidney transplant recipients at 1--year posttransplant, 21% had an eGFR and 40% had mild--heavy albuminuria. The mean age of the cohort was 53 years [IQR 41--62]. Previous thrombosis was higher in recipients with lower eGFR, but previous hemorrhage was similar across all groups. Over a median follow-up of 6 years, the age-- and sex--adjusted rate of hemorrhage and thrombosis was over 2--fold higher in recipients with lower eGFR and mild--heavy albuminuria compared to recipients with higher eGFR and normal albuminuria (hemorrhage: incidence rate ratio, IRR, 2.6, 95% CI 1.5--4.4, p=0.001; thrombosis: IRR 2.3, 95% CI 1.1--5.0, p=0.046). Conclusion: Among kidney transplant recipients at 1--year posttransplant, the risk of hemorrhage and venous thrombosis is higher with lower eGFR and mild--heavy albuminuria. Thus, eGFR and degree of albuminuria may help prognosticate kidney transplant recipients long--term.

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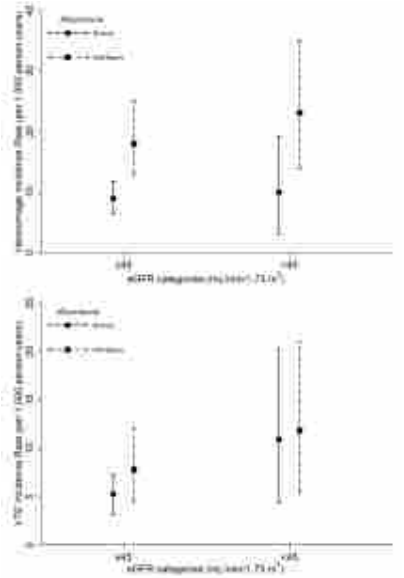

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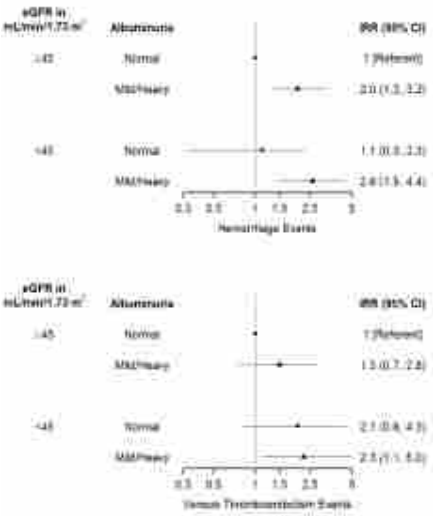

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DraftModeStatus: 0

ID: 87
Biliary intra-operative stents at orthotopic liver transplantation

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: BACKGROUND: Biliary complications can affect 40% of patients after orthotopic liver transplantation (OLTx). Endoscopic management has a high success rate but involves multiple sessions and up to 21% complications. Biliary plastic stents placed manually during OLTx can splint a choledocho-choledochal anastomosis, possibly reducing biliary strictures and leaks. This study evaluates the feasibility and clinical outcomes of ``prophylactic'' intraoperative stenting at a single center, using a propensity-matched analysis. METHODS: All consecutive OLTx patients over a 10-year period are included except for patients with hepaticojejunostomy, fulminant hepatic failure, redo grafts and combined organ transplants. The primary outcome is the incidence of biliary complications (leaks and strictures). Secondary outcomes include: stent morbidity, number of biliary interventions, cholangitis, acute renal failure, graft and patient survival. Propensity scoring was used to diminish selection bias. Outcomes were analyzed for a minimum of 5 years. RESULTS: 265 OLTx patients were included between 2002-2011. 95 patients (36%) received intraoperative stents whereas 170 did not. Age, gender, and medical comorbidities were similar between groups. Total biliary complications (44.2% Vs 44.7%, P=0.94) and biliary stricture rates (45.3%Vs 43.5%, P= 0.79) were similar between groups. However biliary leaks were significantly less frequent in the stented group (2%) vs. non-stented (10%), (P=0.02). Five-year rates of cholangitis, choledocholithiasis, and acute renal failure were similar between both groups. A propensity score model based on multiple covariates including surgeon, year of transplantation and Charlson comorbidity score was used to match 95 patients in each group. The rate of biliary leaks remained significantly lower in the stented group, OR= 0.19 (95%CI= 0.04; 0.86). CONCLUSIONS: Intraoperative use of biliary stents at OLTx is feasible and safe, resulting in less biliary leaks without significantly greater adverse events. 5-year biliary stricture rates appear similar. This study suggests a stenting strategy is feasible and that a randomized trial is worthwhile.

DraftModeStatus: 0

ID: 89
Psychological organ integration among recipients of living and deceased donation

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Member of: CST

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Keywords: transplantation, psychological organ integration, donor representation, fantasized donor, recipient-donor relationship Background. Studies on the psychosocial implications of transplantationsuggest that, while most recipients adapt to their new transplant, the post-transplantation period is challenging and requires considerable adjustment. Studies have mainly focused on outcomes related to psychosocial adaptation (e.g. quality-of-life), with few examining the psychological integration of the organ. Muslin's theory postulated that recipients gradually internalize their transplant, shifting their perception from foreign object to part of their body. Simultaneously, recipients form an imagined representation of the anonymous donor, identical to their self-image at first and gradually distinguished as a separate person. The psychological integration process appears to be an important phase and, if left incomplete, may adversely impact adjustment. This presentation explores the literature on psychological integration of the transplant and attempts to identify themes related to recipients' psychosocial adaptation. Methods. A review was conducted by searching MEDLINE, CINAHL, PsycINFO and WorldCat. Five articles were kept: four on lung and one on heart and kidney recipients. Results. Main themes were: 1) the emotionally-charged nature of the imagined relationship with the deceased/anonymous donor (comprising joy, sorrow, guilt, and gratitude); 2) among recipients of deceased donation, reactions to representations of the transplant and the deceased/anonymous donor are consistently more emotionally-charged compared to living donation; 3) a majority of recipients seem to complete psychological integration, but the minority who persist in perceiving the deceased/anonymous donor in their self-image report more stress, distress, guilt and worries, and the minority who persist in perceiving their organ as foreign report lower compliance. Conclusion.Individual differences in processing a transplant seem to impact recipients' psychosocial adaptation. Further research on this topic is warranted given its clinical relevance.

DraftModeStatus: 0

ID: 90
Oxidative Stress and related responses are induced during ex-situ heart perfusion and may contribute to the functional decline of the ex-situ-perfused heart

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Ex-situ heart perfusion (ESHP), unlike cold storage, preserves the donated heart in a beating, semi-physiologic condition however, myocardial function declines overtime in this setting. We have shown previously that this decline may be a result of the altered energy metabolism. Such alterations may be associated with ESHP-related inflammation and/or oxidative stress. Methods: Porcine hearts were perfused for 12 hours on a custom ESHP apparatus either in non-working mode, (NWM n=5) or working mode, (WM n=5). Cardiac function was assessed during perfusion. The markers of oxidative stress (e.g. malondialdehyde,), the activity of the oxidative stress-responsive pathways/enzymes (e.g. pentose phosphate pathway (PPP), and protein kinase-B (AKT)) as well as activity of creatine kinase (CK) and AMP-activated protein kinase (AMPK) were compared in the left ventricular tissue of the ex-situ -perfused hearts, and in vivo controls (n=4) using immunoassay methods. Results: WM hearts preserved their function better (Figure 1). Malondialdehyde and carbonyl protein levels were higher in ESHP compared to in vivo (p= 0.005 and p=0.02 respectively) and similar in WM and NWM. The activity of PPP and hexosamine biosynthesis pathway (HBP) were significantly higher in ESHP compared to in vivo controls (p=0.03 and p < 0 .001), and HBP activity was higher in NWM (p < 0 .001) (Figure 2A&B). AKT phosphorylation (activation) was induced in ESHP and was higher in WM compared to NWM (Thr308, p=0.03, and Ser473, p=0.01). AMPK and CK activity were lower in NWM compare to in vivo (p < 0 .001 and p < 0 .01) and WM (p=0.001 and p=0.01) and similar in in vivo and WM. Conclusions: ESHP in WM is associated with better functional preservation. The ex-situ perfused hearts were affected by oxidative stress, which may alter energy metabolism and thus myocardial function. Higher CK and AMPK activity, together with lower HBP activity in WM may be associated with the observed superior functional preservation.

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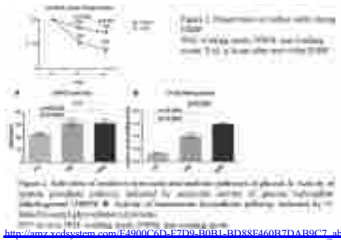

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DraftModeStatus: 0

ID: 91
a case of early active antibody-mediated rejection associated with anti-vimentin antibodies

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Improving precision in predicting alloreactivity is an important unmet need and may require individualized consideration of non-HLA antibodies. Herein we report a 21-year old Caucasian male with ESRD from IgA nephropathy who met all traditional criteria for a “low-risk” transplant for immune memory. He was unsensitized and received a haplotype-matched living donor renal transplant from his mother. There were no anti-HLA donor-specific antibodies (DSA) and flow cross-match was negative. After immediate function, he developed delayed graft function on post-operative day 2. Transplant biopsy showed active antibody-mediated rejection and acute tubular injury with increased vimentin proximal tubular expression compared to the implantation biopsy. He had a history of juvenile idiopathic arthritis and non-HLA antibody screening demonstrated pre-formed anti-vimentin antibody. He was successfully treated with plasmapheresis, IVIg, anti-thymocyte globulin and methylprednisolone with renal recovery. Follow-up biopsy demonstrated decreased vimentin expression with decreased alloinflammation, and graft function remains stable at one-year post-transplant (eGFR 62mL/min). We postulate that pre-formed anti-vimentin auto-antibodies bound to vimentin expressed on apoptotic tubular epithelial cells induced by ischemia-reperfusion injury, and to constitutively expressed vimentin on peritubular capillaries and podocytes. Our case is suggestive of the involvement of antivimentin antibody, whose pathogenic epitopes may be exposed during ischemia-reperfusion injury.

DraftModeStatus: 0

ID: 94
Targeting Th17 cells through inhibition of the nuclear receptor (NR) retinoic acid receptor related orphan receptor γt (RORγt) in highly sensitized renal transplant patients (HSP)

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction: Late and mixed rejections (LMR) are the most common causes of graft loss in transplantation. Currently there is no effective therapy for this condition. T helper 17 (Th17) cells play a major role in the initiation of LMR through the promotion of tertiary lymphoid tissue. Th17 activity is regulated by several transcription factors and by the NR RORγt. Our group has developed a novel class of molecules to target RORγt. We compared in-vitro Th17 polarization in HSP (cPRA=100%) vs non-sensitized renal transplant patients (NSP, cPRA=0%) and tested one of the novel compounds for their effect on cytokine production to validate their proposed effect. Methods: PBMCs from HSP (n=3), NSP (n=3), and healthy volunteers (HV, n=3) were polarized using CD3/CD28 beads, IL6, IL23, IL1β, and TGFβ for 14 days before adding RORγt inhibitor or vehicle for another 48 hours. Intracellular IL17A and IL21 were measured by flow cytometry. Results: Th17 polarization was higher in HSP compared to NSP or HV (figure 1, $p < 0.05$). RORγt inhibitor reduced IL17A and IL21 positive cells compared to controls (figure 2, $p < 0.05$). Conclusion: Inhibition of RORγt may be effective therapy in Th17 mediated LMR. This offers a novel potential targeted therapy for HSP after transplantation.

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Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/94_AbstractImage2_0602042355.pdf

DraftModeStatus: 0

ID: 96
Normothermic ex-vivo kidney perfusion improves function of kidney grafts donated after cardiac death compared to cold storage preservation techniques

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: To increase the donor pool, better preservation strategies for the storage of marginal kidney grafts are crucial. Currently, kidney grafts are either stored on ice (SCS) or perfused at 4 degrees Celsius without oxygen (HMP). Various recent studies showed evidence for improved graft function after transplantation when oxygen is provided during machine perfusion. Moreover, over the last years, a novel technique, normothermic ex vivo kidney perfusion (NEVKP), was developed with promising results regarding graft function and survival. We compared NEVKP with oxygenated HMP (HMPox) and static cold storage (SCS) in a porcine kidney autotransplantation model. Methods: After 30 minutes of warm ischemia, porcine kidneys were removed and either stored on ice or preserved with HMPox or NEVKP for 16 hours, followed by autotransplantation (n=5 per group). Animals were followed for 8 days and graft function was assessed. Results: Postoperative graft assessment demonstrated improved graft function with more rapid recovery for the NEVKP preserved grafts compared to HMPox and SCS groups (mean peak serum creatinine: 3.66+/-1.33mg/dl on POD1, 8.625+/-2.74mg/dl on POD2, and 12.9+/-2.19mg/dl on POD3), respectively. Differences in daily serum creatinine levels are significant between NEVKP and HMPox on day 1 and 2 (p=0.004, p=0.021), between HMPox and SCS on day 3 (p=0.03) and between NEVKP and SCS on days 1 to 4 (p=0.004, p < 0 .001, p < 0 .001, p=0.022). Moreover, on postoperative day 3, creatinine clearance was increased in the NEVKP group. Conclusions: In a DCD model of renal autotransplantation, grafts preserved with NEVKP demonstrated significantly better function compared to both static and machine cold storage. However, grafts preserved with oxygenated HMP showed improvement over SCS. NEVKP appears to offer better preservation in DCD grafts compared to cold preservation techniques.

DraftModeStatus: 0

ID: 98
Donor frailty index – a potential measure of overall donor health status

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Solid organ donors are older and increasingly medically complex, potentially leading to frailty. As frailty confers increased susceptibility to physiologic stress in individuals, donor frailty may predict function of transplanted organ. While organ specific donor risk scores exist, there is no overall donor frailty measure. The cumulative deficits model conceptualizes frailty by counting deficits (eg. abnormal laboratory values, comorbidities) related to health status, creating a continuous frailty index. Our objectives were to create a donor frailty index (DFI), using cumulative deficits, from variables collected before organ procurement and to determine whether frailty correlated with a single donor's number of donated organs, evaluating DFI's concurrent validity. Methods: We performed a retrospective cohort analysis, evaluating 125 variables from 250 organ donors assessments (mean age 48.8, age range 18-86, 62% male, 29% donation after circulatory death (DCD)). We created a DFI using a standardized procedure. Oneway ANOVA correlated frailty with donation type, age and sex. Linear regression determined whether DFI was associated with the number of organs donated per donor. Results: A 28 clinical variable DFI was constructed (mean DFI 0.37, range 0.11-0.64). DFI was similar between sexes but increased with age (Figure 1, p=0.001). Neurological determination of death donors had a higher DFI than DCD donors (mean DFI 0.39 ± 0.10 vs. 0.34 ± 0.10, p=0.002). In univariable analysis, for every decrease in DFI by 0.03, one more organ was donated, (95% CI -0.05 to -0.01, p=0.01). Similarly, adjusting for age, donation type, and sex, one more organ was donated with a decrease in DFI by 0.02 (95% CI -0.04 to -0.003, p=0.022). Conclusions: A DFI can be created from donor data collected before organ procurement. Organ donors with a lower DFI donated more organs, supporting the DFI's concurrent validity. Future studies should assess the DFI's predictive validity for allograft function.

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DraftModeStatus: 0

ID: 99
Association between perceived impact on family, expected health outcomes, and living donor kidney transplant (LDKT) readiness

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: The decision to pursue LDKT is often difficult and patients must weigh several factors, including health outcomes and impact on family relationships. Here we assess the association between patients' perceptions of how the transplant may impact family, perceived health outcomes, and readiness to pursue LDKT. Methods: A cross-sectional, convenience sample of adult patients with end stage kidney disease (ESKD) from dialysis units in Toronto completed the study questionnaire using an electronic data capture system. Participants responded to the questions, "If I got a transplant, my family's life could return to normal", "The surgery will inconvenience the living donor's work or life too much", and "I would live a longer life with a transplant", to assess perceived positive and negative impact on family, and perceived health outcomes (exposure) respectively. We also assessed readiness to pursue LDKT (outcome). Multivariable logistic regression models were used to analyze the associations between exposure and outcome. Results: A total of 485 patients were recruted (63% male, mean [SD] age 57 [14] years); 44% were White, 22% were Asian, 30% were Black, and 4% identified as other. After adjusting for age, marital status, ethnicity, income, comorbidity, and gender, there was no significant association between perceived positive impact or negative impact on family and LDKT readiness. However, high importance of perceived health benefit was strongly associated with being at a later stage of LDKT readiness (OR=3.57, CI=1.69-7.51, p=0.002). When all three variables were included in the regression, only health outcomes predicted LDKT readiness (OR=3.31, CI=1.57-6.97, p=0.002). Conclusion: Patients who saw LDKT as a chance to improve their health were more likely to be at a more advanced stage of LDKT readiness. Emphasizing the significant health benefits of LDKT during transplant education may motivate patients to pursue LDKT.

DraftModeStatus: 0

ID: 100
Long-term outcomes in early allograft dysfunction after liver transplantation in DCD, DBD and living donor grafts

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Early allograft dysfunction (EAD) after liver transplantation has been associated with long-term reduced graft and patient survival. In this single centre cohort study, we aimed to compare incidence, risk factors and outcomes in liver transplant recipients who developed early allograft dysfunction. Methods: Patients who received living donor (LD), donation after circulatory death (DCD) or donation after brain death (DBD) grafts between January 2007 and December 2017 at the University of Toronto were included. EAD was defined as a bilirubin of >10 (171mm/L) or an international normalised ratio (INR) of >1.6 on post-operative day 7 or transaminases >2000 U\l in the first week as previously described. Results: In our cohort of 1485 patients, incidence of EAD was 37.2%. EAD occurred more frequently in the DCD group: 69.7% versus DBD: 40.7% versus LD: 19.9%, respectively (P < 0 .01). Length of postoperative stay on the ICU (2 versus 1 days) and of hospitalization (13 versus 11 days) was significantly longer in the EAD group compared to non-EAD group. Moreover, recipients with EAD showed a significantly lower graft and patient survival at 1-, 3-, and 5-years after transplantation (all p < 0 .001). Overall, multivariate analysis revealed that EAD was significantly associated with DCD grafts, donor age, donor BMI, donor length of stay on the ICU, cold and warm ischemic time (all p < 0 .001). For recipients of LD grafts, predictive markers of EAD were donor and recipient age and recipient diagnose of primary biliary cirrhosis or primary sclerosing cholangitis. In the case of recipients of DBD grafts, predictive markers of EAD were donor age and BMI, recipient MELD score and HCV infection and warm ischemic time. For DCD recipients, donor BMI was associated with EAD. Conclusion: In our cohort study, EAD resulted in poorer long-term patient and graft survival. Predictive markers for EAD are dependent on the donor type.

DraftModeStatus: 0

ID: 101
Immune-Surveillance of Transplant Patients Using a Multi-Omics Approach

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Despite the large number of kidney transplant patients under care, we have virtually no knowledge of the functional recovery of the immune response after transplantation. We aim to enable rapid and innovative monitoring of the dynamic changes in the recipient immune response in organ and cellular transplantation through bioinformatics integration of precise convergent assays for deep phenotyping and cellular bioenergetics. Methods: Peripheral blood of transplant recipients and controls was collected and deep phenotyping was performed using multichannel CytoFLEX cytometry (Coulter) and mitochondrial and cytosolic bioenergetics of T lymphocytes using the Seahorse XFe96 Analyzer (Agilent). Additionally, RNA was stored for transcriptomics. Results: High dimensional flow cytometry: 6 Panels of 55 antibodies provided precise cytometric multichannel definition of innate and adaptive immune cells, for which T-distributed Stochastic Neighbor Embedding (tSNE) and Hierarchical Consensus Clustering enabled automated visualization of surface molecule expression and machine representation of an exceptional array of memory, helper, regulatory and other critical cell subsets. Metabolomics: Mitochondrial and cellular respiration were quantitated by simultaneous measurement of the extracellular acidification rate (ECAR), an indicator of glycolysis and the oxygen consumption rate (OCR) an indicator of oxidative phosphorylation, with and without the use of agents targeting the electron transport chain to determine an array of metabolic parameters including basal respiration, ATP production, maximum respiration and spare respiratory capacity. Conclusion: The combination of deep phenotypic and functional measurements provides a novel foundation for understanding of the changes in the immune system in transplantation. Further phosphoproteomics and transcriptomics will complete multi-parameter monitoring, using bioinformatics integration and visual analytics to streamline clinical interpretation.

DraftModeStatus: 0

ID: 102
Increased mitochondrial metabolic enzymes are associated with superior kidney function after normothermic ex vivo kidney perfusion – a proteomics study

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background Normothermic ex-vivo kidney perfusion (NEVKP) is associated with significantly improved graft function following transplantation in comparison to static cold storage (SCS). We hypothesized that NEVKP would induce key alterations in the kidney proteome compared to SCS, and provide insights into the molecular mechanisms central to superior graft function. Methods Porcine kidneys were removed following 30 minutes of warm ischemia, and then subjected to either SCS or NEVKP (n=5 each) for 8 hours prior to auto-transplantation. Kidney biopsies were collected at time zero, upon reperfusion, and at POD3. We conducted an unbiased proteomics analysis by LC-MS/MS on Q-Exactive-Plus mass spectrometer. Subsequent analyses were performed using MaxQuant, Perseus, R, pathDIP, and NaVIGATOR. Results Kidney function was significantly improved with NEVKP compared to SCS with higher creatinine clearance on POD3. We identified 6354 proteins in total (FDR < 0 .01), with 70 proteins significantly differentially expressed between experimental groups and time points (2-way ANOVA, p < 0 .05) (Fig 1). Gene ontology and enrichment analyses revealed that the proteins increased in NEVKP were associated with the preservation of metabolic processes such as fatty acid ß-oxidation, the TCA cycle and oxidative phosphorylation (e.g. CPT2, MPC2, ETFB). Additionally, proteins associated with the preservation of cell integrity (e.g. CGNL1, PDLIM4) were enhanced in NEVKP in contrast to SCS. Proteins increased in SCS were associated with RNA binding and protein translation. Comparison with external datasets of ischemia reperfusion injury, and datasets relating to other models of acute and chronic kidney injury confirmed that many of the molecular changes observed in these datasets are expected to be reversed or attenuated by NEVKP (Fig 2). Conclusions The proteome-level changes associated with NEVKP demonstrate that the preservation of major metabolic pathways, and of cell polarity and integrity may be pivotal mechanisms by which NEVKP results in improved graft function.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/102_AbstractImage1_0602051847.pdf

Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/102_AbstractImage2_0602051847.pdf

DraftModeStatus: 0

ID: 103
Hypothermic Machine Perfusion Resistive Index as a Predictor of Short and Long-term Renal Allograft Outcome

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Storage of deceased donor kidneys with hypothermic machine perfusion (HMP) permits study of renovascular resistance to continuous perfusion pressure which may be be prognostic of short and long-term graft outcomes. Our objective was to evaluate the effect of the HMP-calculated resistive index (RI) on graft outcomes. Methods: A retrospective review of kidney transplantation from deceased donors between January 2007 to June 2017 from a large single centre was performed. Donor and recipient information was procured from a centrally maintained transplant database. HMP RI values were obtained from paper recordings of RI maintained by operating room staff. RI value at 60 minute was used for analysis as this time point . Results: 156 cases were identified for analysis of which 144 cases were NDD, 12 DCD. Median RI value at 60min on HMP was 0.22 and used as a cut-off value. Univariate analysis showed a significant association between an RI greater than 0.22 and delayed graft function (DGF), (p=0.04) longterm graft failure (p=0.03), and overall survival (OS) (p=0.01). On multivariate analysis, 60min RI remained significantly associated with long-term graft failure, OR 2.24 (p=0.03). Conclusion: Our data suggest that deceased donor kidneys with an RI greater than 0.22 at 60min on HMP have a significantly higher chance of graft failure in longterm follow up. Further investigation into RI dynamics may allow better stratification of donor kidney quality prior to implantation.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/103_AbstractImage1_0602083233.pdf

DraftModeStatus: 0

ID: 104
Subclinical bowel perforation after Kidney Transplant

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Introduction: Infections are the leading cause of hospitalization in transplant recipients. Risk is determined by epidemiologic exposure, immunosuppressive therapy and prophylaxis. The predictable sequence of appearance of infections helps in making management decisions. Case report: We present a 45-year-old male who underwent a preemptive kidney transplant for ESRD secondary to type 1 diabetes, other comorbidities included hypertension, dyslipidemia, and a mechanical aortic valve for congenital bicuspid valve. Eleven days later patient present to his follow-up visit to the clinic completely asymptomatic and his bloodwork demonstrated 22,000 WBC. An unremarkable ultrasound was performed followed by a computer tomography that showed a collection suggestive of small bowel perforation. Patient underwent a midline laparotomy and a perforated appendix and pus were found, appendectomy and lavage were performed and was started on piperacillin/tazobactam. Patient had an uncomplicated recovery and discharged in POD#7 with oral antibiotics and good graft function. Discussion: There are few reports of appendicitis in kidney transplant recipients. Eight patients, all of them adults, have been reported in the literature to date. Appendicitis in kidney transplant recipients is an important diagnosis to make promptly because of the risk of perforation. This disease may be a result of primary infection due to transmission via environmental exposure, or secondary to reactivation of latent infection following immunosuppression. Infection may be asymptomatic, or present with either mild self-limiting febrile illness or severe multisystem disease. Kidney Transplant patients require different suspicion criteria. Renal transplantation is a relatively uncommon clinical subject for the general physicians, who will be unfamiliar with many of the acute problems presenting in a transplant patient. It is uncommon for acute allograft rejection, obstruction, or urinary tract infection to cause these findings. However, acute appendicitis can occur in the transplant recipient just as in the general population; any further delay in diagnosis may complicate

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DraftModeStatus: 0

ID: 105
Assessing the association between sex and access to living donor kidney transplantation (LDKT)

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Background: Published studies suggest that women may experience lower kidney transplant rates than men. LDKT is the optimal treatment option for eligible patients with end-stage kidney disease (ESKD). To determine if women are disadvantaged in accessing LDKT, we assess the association between sex and readiness to pursue LDKT, having a potential living kidney donor (pLKD) identified, and receipt of LDKT offer. Methods: A cross-sectional, convenience sample of adult patients with ESKD from dialysis units in the Greater Toronto Area completed study questionnaires using an electronic data capture system. Clinical data was collected from electronic patient records. Sex was patient-identified (exposure). We assessed readiness to pursue LDKT (outcome) using a standard questionnaire. Participants also indicated if they had a pLKD identified or received an offer of LDKT (secondary outcome). Results: Of the 485 participants (mean[SD] age= 57[14] years), 38% were female, 44% were White, 22% were Asian, 30% were Black, 51% were married, 45% had diabetes, 65% were on dialysis for ≤3 years, and 35% were on dialysis for >3 years. After adjusting for sociodemographic variables, comorbidity, and ethnicity in a multivariable logistic regression model, females were more likely to have a pLKD identified than males (OR=1.7, CI=1.0-2.9, p=0.05). There was no significant difference in stage of LDKT readiness or having received an offer of LDKT between females and males. Conclusion: This study showed that females were more likely to have a pLKD identified, but there was no difference in LDKT readiness or having received an LDKT offer between sexes. Although these results suggest minimal disparities in access to LDKT between sexes in this population, previous studies have shown that women are less likely than men to complete pre-transplant workup or receive LDKT. Future studies should be done in representative samples to confirm our findings.

DraftModeStatus: 0

ID: 106
Giant renal cell carcinoma in transplant kidney. Is immunotherapy a first line option?

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Introduction: Renal cell carcinoma (RCC) in a kidney allograft is rare. Immunotherapy plays a significant role in the management of renal cell carcinoma (RCC) patients with metastatic disease because RCC is highly resistant to both chemotherapy and radiation therapy. National Comprehensive Cancer Network suggest surgery for RCC in non-transplant kidneys. Case report: We present a 44-year-old male who underwent a living related kidney transplant in 1999 for ESRD of oligomeganephronia. On January 2019 presented with a pulmonary embolism (PE) episode and was started on anticoagulation, ultrasound demonstrated a mass on the lower pole of the renal transplant, compatible with neoplasm. Computer tomography and magnetic resonance imaging confirmed a vascularized 10x8x8cm mass (Fig. 1) and paraaortic lymphadenopathy, one measuring 2x3cm. Biopsy of both masses confirmed diagnosis of renal cell carcinoma, classified as stage III-IV. Immunosuppression was held and patient was initiated with check point inhibitors (Nivolumumab and Ipilimumab). One week later presented with fever of 39 and abdominal pain over the graft. Transplant nephrectomy was performed, therapeutic heparin restarted for PE, hemorrhage on postoperative day (POD) #2 and underwent packing. Unpacked 3 days later without further complications. Discharged on POD #16. Discussion: The incidence of de novo carcinomas in kidney allografts is reported to be 0.19–0.5%. The decision to perform surgery or new immunotherapy relies on the specifics of the neoplasm, the size, the location, and if any other structures are compromised. Complications like the one presented here are a consequence of the held immunosuppression and immunotherapy which can be associated to a severe rejection episode and make the surgical process harder as severe inflammation persists in the surrounding tissue.

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DraftModeStatus: 0

ID: 107
Effect of high variability of tacrolimus blood concentrations on graft survival of kidneys with unfavorable donor index.

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction: Tacrolimus (Tac) was first introduced in 1990s and is today the backbone of immunosuppressive therapy after renal transplantation. Given its narrow safety margin, this CNI's levels are frequently monitored to avoid toxicity. However, high variability of tacrolimus blood levels (HVTBL) in recipients has been associated with unfavorable post-transplant outcomes and limited graft survival. To date, there is little information of the impact of HVTBL in patients receiving kidneys from donors with poor KDRI. Methods: Performed at the QEII Sciences center, patients who underwent kidney transplant and tacrolimus was selected and maintained as primary immunosuppressor from 2010-2015 and completed a 3 year follow up. Results: A total of 101 patients were revised. We present with a overall graft surviva of 93% on the first year. TAC variability on the first month reported at 10.7+-3.1. A total of 15% patients presented with KDRI. No statistical significance found in this group. Discussion: As in all observational studies, cause and effect cannot be concluded. Despite this study's limitations, our data is not consistent with previous observations demonstrating a significant association between higher tacrolimus variability and higher rates of renal allograft loss.

DraftModeStatus: 0

ID: 108
Socioeconomic status and access to living donor kidney transplantation

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Background: Inequitable access to living donor kidney transplantation (LDKT) results in inferior clinical outcomes for patients who may be unable to access LDKT due to various barriers. Patients with lower socioeconomic status (SES) have reduced access to LDKT in the US and other countries. The association between household and neighbourhood level socioeconomic factors and access to LDKT has not been well studied in Canada. Here we analyze the association between SES and having a potential living kidney donor (pLKD) identified, a potential marker of access to LDKT. Methods: A cross-sectional, convenience sample of adult patients with end stage kidney disease from dialysis units in Toronto completed study questionnaires using an electronic data capture system. Patients indicated if they had a pLKD identified (outcome). SES (exposure) was assessed by patient-reported information on neighbourhood safety, car ownership, and how long their family could maintain their current situation if their income was lost. Above SES variables along with income, education, employment, and ownership of a washer/dryer were summed to create a composite SES score. Results: A total of 755 participants were recruited (61% male, mean[SD] age: 57[16] years); 48% were White, 22% were Asian, 27% were Black; 39% had type II diabetes, and 38% were on dialysis for >3 years. After adjusting for demographic variables, comorbidity, ethnicity, and immigrant status in a multivariable logistic regression, higher neighbourhood safety (OR=1.9, CI=1.1-3.3, p=0.02), car ownership (OR=2.9, CI=1.9-4.6, p < 0 .001), and better overall SES (OR=4.0, CI=1.6-10.1, p=0.008) were significantly associated with having a pLKD. Conclusion: In our analysis, higher neighbourhood safety, car ownership, and overall SES were associated with increased odds of having a pLKD identified, indicating the significant role of individual, household and neighbourhood-level socioeconomic factors on access to LDKT. Future work should be aimed at interventions to reduce socioeconomic disparities in access to LDKT.

DraftModeStatus: 0

ID: 109
Targeting latent cytomegalovirus in donor lungs with a novel fusion toxin protein using ex vivo lung perfusion as a platform

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

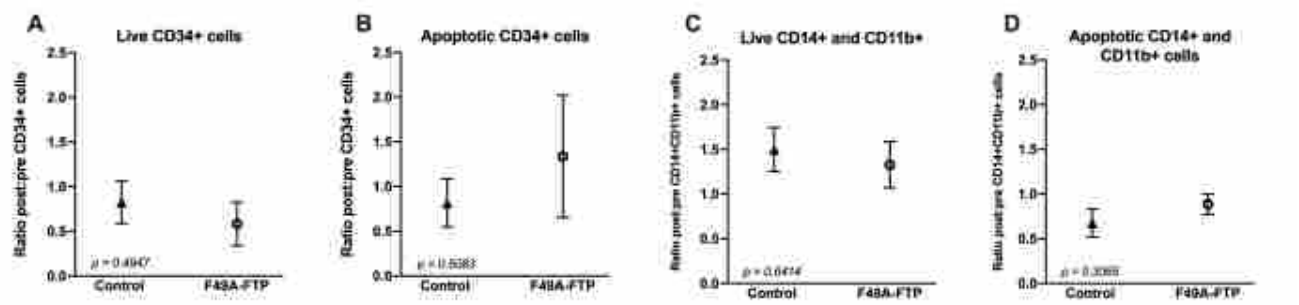
Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Donor to recipient human cytomegalovirus (CMV) mismatch leads to high incidence of CMV infection post lung transplant causing devastating impact in patient outcomes. Ex-vivo lung perfusion (EVLP) is a potential platform to repair grafts prior to transplantation. We hypothesized that EVLP delivery of F49A-FTP, a fusion toxin protein that targets with ultra-high affinity cells expressing the latent CMV protein US28, may safely clear latent CMV from donor lungs, thus attenuating viral reactivation post-transplant. Methods: Human donor lungs rejected for transplantation were randomly placed on EVLP alone (n=3) or EVLP with 1mg/L of F49A-FTP (n=4) for 6 hours. Since F49A-FTP induces apoptosis of the cells expressing US28 (CD34+ stem cells and monocytes/macrophages), flow cytometry was used to quantify the proportion of these cells in lung tissue collected pre and post perfusion. Lung viral burden was quantified through RT-qPCR measurements of US28. Lung physiology was monitored to evaluate possible acute deleterious effects of F49A-FTP. Results: F49A-FTP was delivered through lung vasculature on EVLP and no evident toxic adverse events were noticed. The ratio of post to pre perfusion CD34+ and CD14+CD11b+ cells was used to assess the efficacy of F49A-FTP to kill infected cells. Treatment lungs showed a trend towards decreasing live CD34+ cells and increasing apoptotic CD34+ post perfusion when compared to control lungs: live 0.6±0.5 vs 0.83±0.6,p=0.4947and apoptotic1.4±1.5 vs 0.8±0.6,p=0.5083 (Figure 1). When analyzing CD14+CD11b+ cells, the same effect was not noticed. However, interestingly a 5-fold decrease in US28 levels was observed in the F49A-FTP group compared to only 0.4-fold decrease in control (Figure 2). Conclusion: Initial results from our study show that F49A-FTP has the capacity to decrease CMV latent burden in donor lungs using EVLP with no evident acute toxic effects.

Abstract Image 1:



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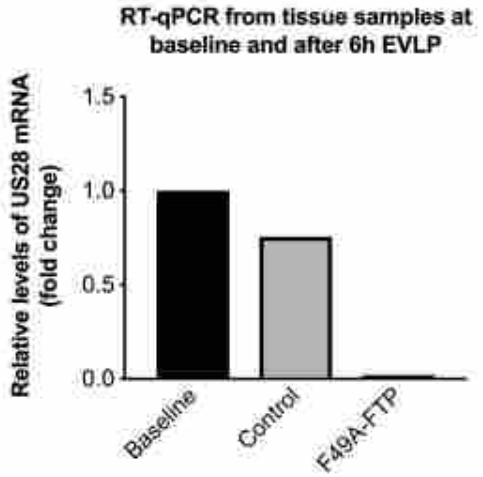

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DraftModeStatus: 0

ID: 110
The perspective of families regarding their decision to donate a loved one's organs

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background The decision to donate is typically made in a context of crisis, over a short time. Organ procurement organizations stress that families must feel free to make their own decision to feel at peace and harbor no regrets afterwards. However, few studies have examined how families continue to live with their decision. The purpose of the present study is to get a better understanding of how families feel and make sense of their decision after agreeing to donate the organs of a loved one. Methods Qualitative interviews were conducted separately with 16 individuals from 12 families who were involved in decision-making and agreed. They were interviewed 6 months to 5 years after donation. Data were analysed based on Interpretative Phenomenological Analysis, which offers an in-depth insight into how individuals make sense of an experience. Results Data suggested that several elements influence how families view and deal with their decision. Three factors appear to influence positively families' serenity with their decision: (1) being aware of the deceased's wishes regarding donation, (2) believing that the deceased person continues to live through the donation and (3) perceiving the gesture as the only positive element under the circumstances. For families who remain ambivalent, central elements in their discourse include doubt regarding their loved one's wishes, not having a clear understanding of the medical procedures involved in the donation process and not knowing what happened with the organs afterwards. They lacked a sense of closure and missed important information. Conclusion The results suggest that while all families affirm they made the right decision, many still have questions and struggle with negative emotions years after. This suggests a need to follow up on families to answer questions they might have and provide them with support through the mourning process.

DraftModeStatus: 0

ID: 111
Gaseous Nitric Oxide (gNO) as a potential antimicrobial therapy during ex vivo lung perfusion

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

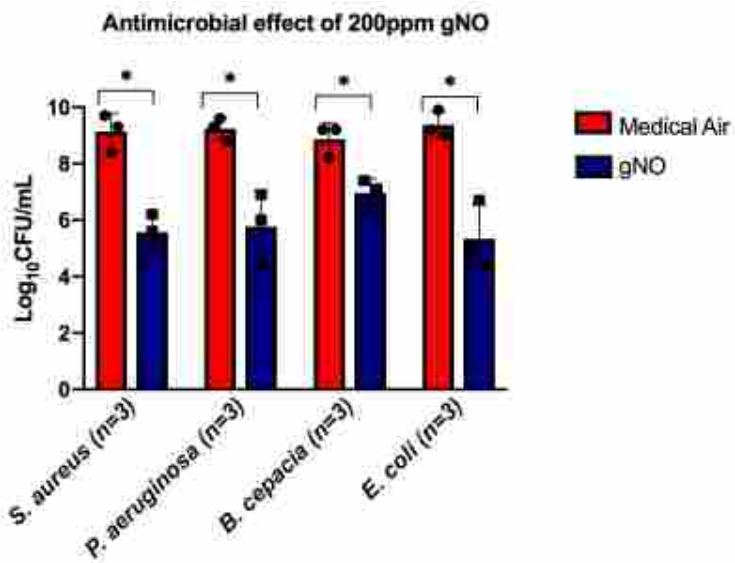
Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Lung transplantation is a lifesaving procedure for patients with end-stage lung diseases. Normothermic ex-vivolung perfusion (EVLP) is a well-established clinical platform to evaluate grafts prior to transplantation and has been used to treat infection in donor lungs with high dose of antibiotics successfully. However, with the increase of antimicrobial resistance it is crucial to develop alternative therapies. Nitric oxide (gNO) has antimicrobial effect against a several microorganisms. So far no previous attemps have been made to examine the potential use of gNO on lung infections using EVLP as a platform. Experiments using ATCC strains of P. aeruginosa, S. aureus, E. coli and Burkholderia cepacia were performed. Agar plates were inoculated and transferred into either control or treatment chamber. Medical air was used at constant flow of 10 L/min for both groups and high-pressure cylinder of NO (Praxair, ON, CA) was delivered to the treatment chamber using a digital gas regulator at 200ppm. Gas concentration was checked with AeroNOx machine. Gaseous NO was delivered for 6 hours in the treatment chamber with a constant concentration of 200ppm ±10ppm and NO2levels were < 2.5ppm. Regarding bacterial growth, gNO reduced successfully all bacteria strains when compared to control (n=3 each strain): P. aeruginosa (5.8 ±1.27 vs 9.2 ±0.40 Log10CFU/mL, p= 0.01),S. aureus (5.6 ±0.65 vs 9.1 ±0.66 Log10CFU/mL, p= 0.002), E. coli (5.3 ±1.20 vs 9.4 ±0.47 Log10CFU/mL, p= 0.005) and Burkholderia cepacia (7.0 ±0.51 vs 8.9 ±0.57 Log10CFU/mL, p= 0.01) Figure 1. Continuous gNO at 200ppm has potential antibacterial activity against gram – and + strains. In this study we evaluated the effect of gNO towards common respiratory pathogens in vitroas a proof of concept to apply inhaled NO during EVLP in the near future.

Abstract Image 1:



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DraftModeStatus: 0

ID: 112
Kidney Transplantation in Older Recipients from Expanded Criteria Donors

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Introduction: The disparity between kidney supply and demand for transplantation has prompted the use of kidneys from expanded-criteria donors (ECDs) which may have shorter graft survival. Our objective was to compare long-term patient and renal allograft outcomes in recipients receiving kidneys from standard criteria (SCD) or ECD kidneys, with a focus on older (>65yr) recipients. Methods. We retrospectively reviewed all deceased-donor kidney transplantations performed from January 1967 to December 2017 at a single large academic institution. Standard donor and recipient characteristics were collected from a central transplant database. Recipients were divided into older and younger groups and stratified by donor type: ECD vs SCD. DGF is defined as a need for dialysis or a failure of the serum creatinine to drop by >10%, in the first post-operative week. Results: 2790 renal transplant cases were identified, with 1838 SCD and 952 ECD cases. Overall death-censored graft survival of the entire cohort was 158.57 ± 4.29mo, with 178.33 ± 5.43mo vs 114.40 ± 5.45mo for SCD vs ECD, respectively (p 65yrs at the time of transplant with mean age of 69 years. Median overall survival (OS) and median graft survival for this age group was 152.6 ± 23.4mo and 136 ± 18.4mo for SCD vs 95.8 ± 9.1mo and 90.2 ± 5.9mo for ECD (p 65 who died, 98% had a functioning graft. Conclusion: Our data suggest that older recipients receiving an ECD kidney have a shorter graft survival compared to SCD kidneys, however this effect may be driven by patient factors, as most individuals have a functional graft at time of death.

DraftModeStatus: 0

ID: 114
Kidney transplant (KT) education in renal programs using on-line resources – interim report

Member of: CST

Abstract Type: Adult Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Limited knowledge about KT may prevent patients with chronic kidney disease (CKD) from pursuing KT. To promote KT education in Ontario CKD programs we made the Explore Transplant Ontario (ETO) transplant education program available on-line for patients and nephrology staff. In conjunction, we started a webinar series to inform staff about KT. We report preliminary data about the utilization of these resources. Methods: The Explore Transplant package consists of four videos and accompanying information brochures. The videos include personal testimonials from KT recipients and donors alongside factual information about KT. ET was adapted for use in Ontario by a working group of patient representatives, nephrology and KT professionals. ETO has been made available for patients and staff in 13 of Ontario's 27 regional CKD programs as part of a multicomponent, quality-improvement initiative. CKD programs received physical ETO packages and specific website credentials, enabling us to monitor usage and differentiate between patient and professional users. Results: We have distributed over 5000 ETO packages since October 2017, when the project was launched. We registered ~ 2000 patient and ~2500 healthcare provider access events to ETO online. Furthermore, >300 professionals attended the live or archived staff webinars. There was substantial variability in the site usage between CKD programs, only partially explained by program size. Furthermore, programs differed in proportion of use by professionals versus patients. Cumulative usage has been steadily growing for patients and increased sharply for professionals following launch of the webinars. Anecdotal feedback from patients and professionals indicated that the website was useful in attaining KT information. Conclusion: The ETO website has been well utilized and received by patients and nephrology professionals. Future directions include analysis of usage and potential associations between website use, access to KT and practice changes.

DraftModeStatus: 0

ID: 115
Human islet extracellular vesicles induce proinflammatory signalling in monocytes via toll-like receptors

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Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Background: The distinct events involved in the generation of an autoreactive immune response in type 1 diabetes (T1D) are not well understood. In both physiological and pathological conditions, cells release a variety of signals, including extracellular vesicles (EV). Previous work in our laboratory has identified that human islets release EV containing islet autoantigens that are taken up by monocytes and elicit pro inflammatory responses in T1D PBMC. However, the mechanism by which EV interact with monocytes remains unknown. It has been shown in other disease contexts that EV activate monocytic cell lines via toll-like receptor (TLR) signalling. Here, we aim to investigate the role of TLR in islet EV-mediated monocyte activation. Methods: Human islets were isolated from multi-organ donor pancreases. Islets were cultured for 24 hours and EV were purified from conditioned media by sequential centrifugation. Peripheral blood mononuclear cells (PBMC) were isolated from healthy controls (HC) by Ficoll. PBMC were treated with EV and/or CLI-095 (TLR4 inhibitor) or OxPAPC (TLR2/TLR4 inhibitor) prior to stimulation with EV. Analyses were conducted using flow cytometry to assess proliferation, cell surface markers and intracellular cytokine staining in response to EV. Statistical analyses were performed via t-tests and ANOVA. Results: We show that EV are readily taken up by CD14 monocytes in both total PBMC and isolated monocytes. We demonstrate that EV stimulation triggers an increase in HLA-DR, IL-6 and TNF-a expression in CD14 monocytes. To investigate the effect of EV on TLR, PBMC were pre-treated with CLI-095 or OxPAPC. Treatment with CLI-095 decreased HLA-DR, IL-6 and TNF-a MFI in CD14+ monocytes, which was further reduced with OxPAPC treatment. Conclusion: We show that TLR are implicated in EV-mediated monocyte activation. Advances in this field may help to better characterize the mechanisms by which islets and immune cells cross talk to generate islet specific

DraftModeStatus: 0

ID: 116
Policy Challenges for Organ and Tissue Allocation in an Era of "Precision Medicine"

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Health care systems around the world are increasingly embracing evidence-based outcome measures and the use of precision medicine tools for donor-recipient matching to maximize utility related to graft survival. While the shift toward greater precision clearly provides health and resource benefits, the concomitant emphasis on utility can also create a range of policy concerns relating to, among other things, equity. Methods: We used traditional methods of legal scholarship, including review and analysis of legislation, case law, policy and related academic texts to identify and explain key policy challenges relating to increasing precision in allocation. Results: We identified several challenges. First, professional obligations of healthcare providers to patients include (in Canada) an ethical requirement to place the best interests of patients above those of the broader health system. This "rule of rescue" is at odds with increasingly precise allocation technologies, and some physicians have already "gamed the system" to improve their patients' opportunity to receive an organ. Second, increased precision in allocation that does not have robustly proven clinical relevance may be impeded by right of access litigation or claims of genetic discrimination by those who may benefit from an organ but fall outside of tighter new criteria. Third, public perceptions and popular representations have tended to favour a patient access ethos, and if these perspectives are not sufficiently reflected in allocation decision-making, social pressure could mount in opposition to new precision metrics. Conclusion: Multiple policy challenges could impact the adoption of precision medicine allocation tools in a clinical context. Overcoming these challenges could involve altering longstanding policy, public education campaigns, and/or modifying the application of new precision technologies to accord with policy and public perceptions.

DraftModeStatus: 0

ID: 117
A Reduced Intensity Conditioning Protocol Induces Chimerism and Transplant Tolerance to Fully Allogeneic Islets in Autoimmune Diabetic NOD Mice

Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Background: A reduced intensity conditioning protocol is desired for inducing hematopoietic chimerism, the most efficacious method for generating tolerance to donor organs. We previously showed that donor chimerism is achievable in pre-diabetic, non-obese diabetic (NOD) mice with a T cell depletion based conditioning protocol. Here, our goal is to develop a protocol for inducing chimerism and tolerance to allogeneic islets in NOD recipients that have become diabetic, which is believed to be an even more challenging model. Methods: We preconditioned pre-diabetic and spontaneously diabetic NOD mice with lymphocytes from fully mismatched FVB mice (d-10), cyclophosphamide (d-8), antibodies against CD4/8/90 (d-6, -1, 4, 9, 14), and busulfan (d-1). FVB islets and/or bone marrow transplantation (BMT) were done at d0. FVB CD8α cells were injected in a group of diabetic mice at d19. Blood glucose was assessed weekly. Flow cytometry was used to detect chimerism. Results: We determined that age rather than overt diabetes is associated with the resistance to chimerism. We induced transient chimerism in old-diabetic NOD mice with significantly prolonged survival of donor islets in chimeric mice. Recipient T cells in diabetic NOD mice were depleted as efficiently as in pre-diabetic NOD mice but rebounded quickly. Levels of chimerism and donor T cells were lower in diabetic recipients at early time points compared to young pre-diabetic NOD mice. The delayed infusion of donor CD8α cells facilitated the establishment of a high level and stable multilineage donor chimerism and the acceptance of donor islets without the presence of graft versus host disease. Conclusion: A T cell depletion based chimerism protocol induces chimerism in diabetic NOD mice and promotes tolerance to fully allogeneic islets.

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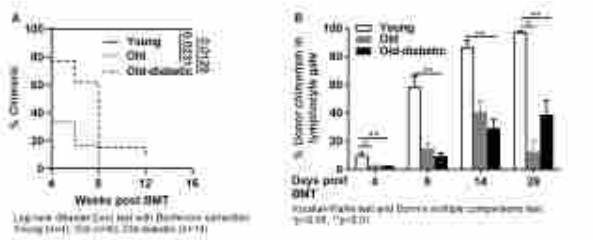

Fig1. Age rather than overt diabetes is associated with resistance to chimerism. Young (n=4), Old (n=6), or Old-diabetic (n=14) NOD recipients were conditioned with DST (day −10), CYP (day −8), a combination of anti-CD4/8/CD90 mAb (days −6, −1, 4, 9, 14), busulfan (day −1), and bone marrow cells (day 0, 20×10^6). Recipients were considered chimeric when at least 5% of MHC-I$^+$ cells in the lymphocyte gate were donor derived at day 28 post-BMT. (A) Shown are proportions of recipients that became chimeric at day 28 post-BMT and maintained chimerism thereafter. (B) Shown are the proportions of donor cells in lymphocyte gate in peripheral blood lymphocytes at each time points post BMT.

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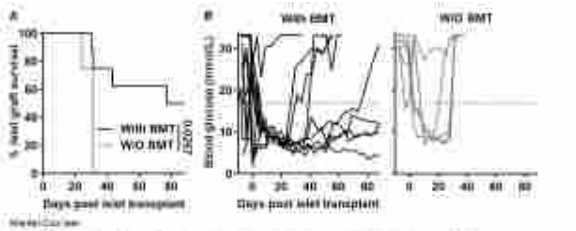

Fig2. BMT can significantly prolong the survival of donor islets. Old-diabetic (n=14) NOD recipients were conditioned with DST (day −10), CYP (day −8), a combination of anti-CD4/8/CD90 mAb (days −6, −1, 4, 9, 14), busulfan (day −1), and islet transplant with 500 FVB islets (day 0). Bone marrow transplant (day 0, 20×10^6) were performed in 9 recipients. (A) Shown are proportions of recipients that became and maintained euglycemia. (B) Shown are blood glucose levels before and after islets transplant.

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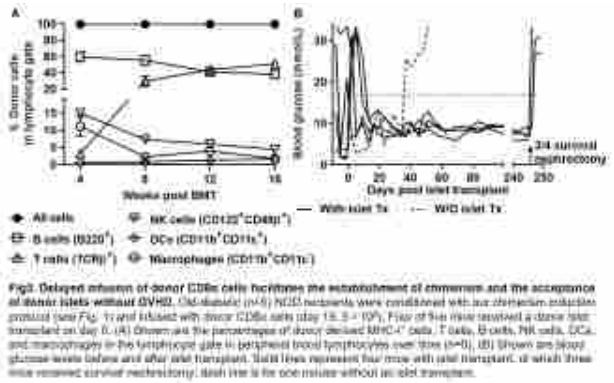

Fig3. Delayed infusion of donor CD8α cells facilitates the establishment of chimerism and the acceptance of donor islets without GVHD. Old-diabetic (n=5) NOD recipients were conditioned with our chimerism induction protocol (see Fig. 1) and infused with donor CD8α cells (day 19, 5×10^6). Four of five mice received a donor islet transplant on day 0. (A) Shown are the percentages of donor derived MHC-I$^+$ cells, T cells, B cells, NK cells, DCs, and macrophages in the lymphocyte gate in peripheral blood lymphocytes over time (n=5). (B) Shown are blood glucose levels before and after islet transplant. Solid lines represent four mice with islet transplant, of which three mice received survival nephrectomy; dash line is for one mouse without an islet transplant.

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DraftModeStatus: 0

ID: 118
Validation of Social Difficulty Inventory (SDI) in Kidney Transplant Recipients (KTR)

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Kidney transplant recipients (KTRs) may experience psychosocial distress, that is frequently un-noticed and un-managed. The Social Difficulties Inventory (SDI) has been developed to assess social difficulties in patients with cancer. Here we evaluate the validity of SDI in KTRs. Methods: A cross-sectional, convenience sample of˙adult KTR completed the SDI, the Generalized Anxiety Disorder7 and the Patient Health Questionnaire9, ˙using electronic data capture. Clinical characteristics were collected from medical records. The SDI contains 21 questions, 16 of which load on a single factor and form the SDI-16 score. It also has three subscales: "Everyday Living", "Money Matters" and "Self and Others". Internal consistency and convergent validity were assessed with Cronbach's alpha and Spearman's Rho, respectively. Structural validity was evaluated with confirmatory factor analysis (CFA). Construct validity was examined assessing associations with questions about financial stability and neighborhood safety. Results: Of˙251 participants (mean (SD) age 52(16) years) 58% were male and 63% were Caucasians. Internal consistency of the "everyday living", "money matters" and "self and others" subscales (α =0.87, 0.85 and 0.82, respectively) and of the SDI-16 (0.91) was very good. CFA demonstrated good model fit for SDI-16 and the subscales. The SDI-16 score was moderately correlated with depression (Rho=0.62) and anxiety (Rho=0.61) ($p < 0.001$ for both). The SDI-16 score was higher in patients with low vs higher financial stability (median [interquartile range – IQR] 6[2, 16] vs 3[0, 9]$p < 0.05$) and low vs higher neighbourhood safety (10[5, 18] vs. 3[1, 7.5], $p < 0.001$). Similar associations were seen between SDI subscale scores and other measures of SES. Conclusions: This study provides data about the validity and reliability of the SDI to assess social difficulties in KTR. Further work is needed to determine the benefit of referring patient patients with significant social difficulties to additional support services.

DraftModeStatus: 0

ID: 119
ABO-antibody detection: Development of a complete ABO A and B bead-based assay

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Member of: Student/Others

Abstract Type: Pediatric Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Heart

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND: ABO-incompatible (ABOi) pediatric heart transplantation is a safe way to increase the donor pool for infant heart transplantation. However, the assay used to measure ABO antibodies in ABOi cardiac transplantation is inadequate for ABH subtype antibody specificity and isotype analysis and is thus limited for ABOi transplantation assessment. We developed a slide glycan microarray, which is an excellent tool for the fine characterization of ABO antibodies, but has limitations for implementation in the clinical lab. The goal of this study was to complete the development of Luminex, single subtype antigen ABO A and B panels and use these tools to measure ABO-A and B antibodies in healthy adult controls. METHODS: Blood group subtypes A-I through A-VI and B-I through B-VI were conjugated to bovine serum albumin (BSA) then coupled to Luminex beads. Success of coupling was confirmed using monoclonal antibodies. These ABO A and B panels were used to measure ABO antibody in healthy adults (n=28); glycan array testing was performed for comparison. RESULTS: Complete A and B panels were successfully coupled to Luminex beads. Glycan array and Luminex methods demonstrated similar MFI values for ABO-A IgG antibody detection (Figure1). The Luminex method appeared to provide increased differentiation of antibody to IgM ABO A (Figure1) and ABO-B IgG and IgM B (Figure2). Some normal controls demonstrate more IgM to IgG isotype switching for both ABO A and B antibodies (Figure3). CONCLUSION: This bead-based assay enables measurement of ABO-A and B subtype antibody specificity and isotype. The assay has rapid turn-around and can be read on existing equipment in the clinical lab facilitating easily adoption in the clinical laboratory, where the technical expertise to run this assay already exists. The Luminex bead-based assay for ABO antibody characterization offers a promising alternative to isohemagglutination for use in ABOi transplantation.

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Abstract Image 3: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12578/119_AbstractImage3_0602101550.pdf

DraftModeStatus: 0

ID: 120
The Impact of Weight Reduction Surgery and Morbid Obesity on Renal Function after Transplantation.

Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Morbid obesity is a significant barrier and renal transplantation is rarely offered to patients with Class III obesity (body mass index (BMI) over 40 kg/m2). Few studies have looked at the effect of pre-transplant surgical weight loss on post-transplant outcomes. Bariatric surgery (BS) especially laparoscopic sleeve gastrectomy (LSG) has been safely used in dialysis patients. In the past decade, patients with a BMI>40 and BMI>35 with 2 comorbidities have been referred for LSG prior to renal transplantation. Prior to this, our center rarely listed patients with BMI>40. We examined the impact of LSG on short term outcomes following renal transplantation (RTx). Methods: All patients undergoing RTx (multiorgan Tx were excluded) between Jan-2010 and Dec-2018 were studied (N=894). BS was performed on 42 dialysis with BMI>40 or BMI>35 with 2 or more comorbidities. 22 underwent subsequent RTx. We compared 3 groups:BMI 30 (obese O, n=244), BMI>30 and Bariatric surgery (OBS, n=22) for immediate renal function post RTx. Success was defined as a eGFR >30ml/min in the first 90 days post RTx or a renal function recovery >70% (RFR = eGFR recipient/(0.5 eGFR donor)*100) during the first 90 days post RTx. Univariate and Multivariate logistic regression was used for data analysis. Results: There were no differences in the baseline characteristics (Table 1) between groups except for more DCD in the OBS group. BS was successful in weight reduction from a BMI of 43.9 to 33.3 (table 1). A higher percentage in NO and OBS groups achieved success in the first 90 days post RTX compared to O group (92%, NO; 91%, OBS vs 82% O. $p < 0.01$) . Conclusion. BS prior to RTx was feasible and successful for most patients and may offer better transplant outcomes. It should be considered as a tool to increase RTx eligibility.

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DraftModeStatus: 0

ID: 121
Does development of a young adult transplant clinic improve outcomes in young adult kidney transplant recipients?

Member of: Student/Others

Abstract Type: Pediatric Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Poster/E-Poster only

Trainee: Yes

Abstract Body: Introduction: Young adult kidney transplant recipients have one of the highest rates of rejection leading to graft loss. In November 2011, a multidisciplinary young adult transplant clinic (YATC) for ages 18-26 was implemented to improve the transitional process from pediatric to adult care and to deliver developmentally appropriate care with educational and social supports. We hypothesized that YATC patients would experience less rejection episodes and improved adherence than patients transitioned to regular adult care before November 2011 (non-YATC). Methods: A retrospective chart review was conducted for the 3 years after transfer into either YATC or non-YATC. Demographic data, time post-transplant and age at transition was documented. Number of clinic visits, emergency department (ED) visits, hospitalizations, monthly lab tests, biopsy proven rejection (BPAR) and graft failure data were collected during the 3 year period. Means and frequencies were compared between groups. Results: 39 patients (20 female); n=22 YATC, 18.3±0.8 years at transition and n=17 non-YATC, 18.7±0.6 years at transition. Time post-transplant at transition: YATC 4.4±3.6 years, non-YATC 4.6±4.1 years. YATC patients attended 2.9±0.6 transplant clinics/year vs non-YATC 2.3±0.6. YATC group completed 7.4±2.6 monthly lab tests/year while non-YATC completed 7.2±2.5. During the 3 year period, YATC patients had 13 ED visits while non-YATC 16 ED visits. 36% of patients were hospitalized at least once in the YATC group and 35% in the non-YATC group during the 3 year period. YATC had 3 BPAR in 2 patients while non-YATC had 7 BPAR in 5 patients. There were 2 graft failures in YATC; 15.3 and 17 years post-transplant, non-YATC had 2 graft failures; 6.1 and 7.9 years post-transplant. Conclusion: A number of key indicators point to a positive effect of the YATC clinic at our center. Further statistical analysis needs to be completed to evaluate the outcomes experienced in both groups.

DraftModeStatus: 0

ID: 122
Long term outcomes after Adult to Adult Liver Transplantation of deceased donor and living donor; Cumulative single-center retrospective cohort study of 19 years

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Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background The difference between Living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) regarding long-term survival and cause of death is still under discussion. This is a retrospective cohort study to summarize the cumulative 19 year-experience of our liver transplant program as a large Western single center series. Methods We analyzed primary adult-to-adult liver transplants between January 2000 and September 2018. The primary endpoint was to compare the long-term patient and graft survival rate of LDLT and DDLT, and identify causes of death in both groups. Results A total of 2144 patients were enrolled in this study: 628 patients receiving a right lobe LDLT were compared with 1516 patients having a full size DDLT. Differences were present regarding the underlying liver disease diseases (P < 0.0001) and more patients were transplanted with hepatoma in the DDLT group (25.8% vs. 44.6%, P < 0.0001). Compared with DDLT, LDLT patients had tendency of lower MELD score (17.1 vs. 19.0, P = 0.055) and shorter waiting time from listing (211.4 vs. 268.0 days, P = 0.078). No donor death was observed in LDLT. LDLT patients demonstrated significant a higher survival rate and the recipient survival rates at 10 and 15 years were 73.4% and 57.6% in LDLT group, vs 66.6% and 53.4% in DDLT respectively (P = 0.024) (Fig.1). There was no significant difference in graft survival (P = 0.372) (Fig.2), however LDLT was associated with a higher re-transplantation rate (6.7% vs. 2.5%, P < 0.0001). No difference was observed regarding the cause of death between LDLT and DDLT patients during the follow-up (all term: P = 0.078, after 5 years of transplant: P = 0.062, after 10 years of transplant P = 0.409) (Fig.3). Conclusions Despite different backgrounds, LDLT and DDLT offer similar long-term outcomes in a selected patient cohort.

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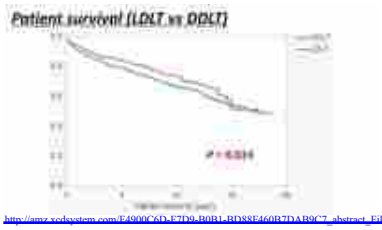

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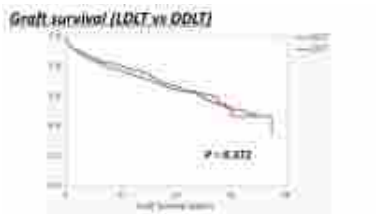

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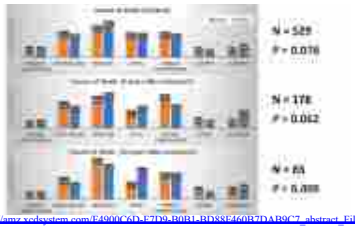

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DraftModeStatus: 0

ID: 123
Donor-specific chimeric antigen receptor Tregs restrain rejection in naive but not sensitized allograft recipients

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Member of: CDTRP

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Cell therapy with autologous regulatory T cells (Tregs) is feasible and safe in solid organ transplantation. Phase II trials which aim to combine Treg therapy and immunosuppression minimization are planned but the ability of Treg cell therapy to limit the increased risk of humoral alloreactivity that comes with lower immunosuppression is unknown. We analyzed the effect of irrelevant or donor specific chimeric antigen receptor (CAR) Tregs on humoral alloreactivity in immunocompetent mice receiving skin allografts. Methods: Tregs expressing an anti-HLA-A2-specific CAR (donor specific) or an anti-HER2 CAR (irrelevant) were administered to Bl/6 mice at the time of transplanting an HLA-A2+Bl/6 skin graft in the absence of immunosuppression in naive or sensitized mice. After three weeks, the amount of antigen-specific B cells, T cells and donor-specific antibodies were evaluated. Results: We found that donor-specific CAR-Tregs, but not irrelevant CAR Tregs, significantly delayed skin allograft rejection. Moreover, only treatment with donor-specific CAR-Tregs resulted in diminished levels of transplant-induced donor-specific antibodies (DSAs) and frequencies of DSA-secreting B cells. Donor-specific CAR Tregs-treated mice also had weaker DSA-specific recall antibody response, but normal responses to an irrelevant antigen, demonstrating antigen-specific suppression. When donor-specific CAR Tregs were tested in HLA-A2 sensitized mice, they were unable to delay allograft rejection or diminish DSAs, possibly due to trogocytosis of HLA-A2 and antibody-mediated CAR-Treg clearance. Conclusion: The finding that donor-specific CAR-Tregs restrain de novo but not memory alloreactivity has important implications their use in transplant recipients.

DraftModeStatus: 0

ID: 124
Predicting wait time to a next offer when a first kidney offer is refused

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Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: The aim of this study was to develop and validate a model that could yield individual predictions of wait-time to next offer if an initial kidney offer is refused in the Province of Quebec. Methods: We performed a retrospective cohort study using data on deceased donors and adult kidney transplant candidates available from Transplant Québec (TQ), our provincial organ donation organization (ODO), between March 29th, 2012 and December 13th, 2017. TQ's allocation score gives points for time on dialysis, HLA-DR matching, recipient age, donor-recipient age match, and elevated cPRA. We used a Poisson regression with varying parameters to provide personalized estimates of the time to a next offer based on the TQ score. The predictions were based on the rate of arrival of donors that could have been offered to a recipient in the 2 years previous to each actual offer. Results: Most recovered kidneys were distributed in the general attribution system (Figure 1). Calculations assumed that during wait time post refusal of a first offer, the patient would remain alive and not be permanently withdrawn from the wait list (Figure 2). Our approach allowed for an individual prediction of the median time to the next offer, and a time within which there is a 95% certainty that a next offer will be made. The model performed well with a C-index of 0.72. Time predictions were compared to actual values on the validation set, leading to good results for short time predictions and less precise predictions when predicted wait time was longer (Figure 3). Conclusion: We have developed a model that provides an estimate of wait time prolongation if a kidney from a deceased donor offered by TQ is refused. This information can help transplant physicians and candidates weigh the consequences of refusing an offer.

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DraftModeStatus: 0

ID: 126
Donor Age Supersedes the Impact of Donor-Recipient Size Mismatch on Kidney Graft Survival

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Small donor body size relative to recipient body size is associated with a higher risk of graft failure. Other strong risk factors for graft loss may modulate the relationship between donor-recipient size mismatch and graft survival. The aim of this study was to determine whether the relationship between donor-recipient size mismatch and graft survival is modified by donor and/or recipient age. Methods: This was a retrospective cohort study of all first, single, deceased donor kidney transplant recipients aged ≥ 18 years recorded in the Scientific Registry of Transplant Recipients (SRTR) January 1st, 2000 to March 1st, 2018. We fit multivariate Cox regression models to assess the association between donor-recipient size mismatch (defined as the donor:recipient body surface area (BSA) ratio and categorized as 50 years) and increasing donor age (Figure 1). Model-based estimates of 5-year death-censored graft survival probabilities (Table 1) show that survival probabilities for a size mismatched (donor-recipient BSA ratio < 0 .8) donor aged < 40 years were equal to or better than those for a size matched (donor-recipient BSA ratio ≥1) donor aged ≥ 40 years. Conclusion: Donor and recipient age modulate the deleterious impact of donor-recipient size mismatch on graft survival. Outcomes are equal or superior when accepting size-mismatched kidneys from younger donors vs. kidneys that are not size-mismatched from older donors.

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DraftModeStatus: 0

ID: 127
Phylogenetic template of The Epstein Barr Virus Nuclear Antigen 1 and Associated Correlates Among Canadian Transplant Patients

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: To facilitate an improved understanding of the effect of genetic diversity of the Epstein-Barr virus (EBV) in the transplant setting, we have developed a dynamic phylogenetic tree using the EBV EBNA1 gene; new strains are added to the tree as they are identified. Methods: We examined the variants of the EBNA1 gene among (N=44) patients enrolled in the CNTRP POSITIVE Study of patients (< 1 8 years old) with and without PTLD. The EBNA-1 gene was sequenced from blood samples during EBV DNAemia. Publicly available PTLD sequences and sequences from Canadian patients with infectious mononucleosis (IM) were used for comparison. Sequencing was done by dideoxy DNA sequencing methodology and the sequences were aligned with a reference strain of EBV (B95-8). EBNA1 variants were classified into prototype (P) and variant (V) strains, based on the amino acid change that occurred at codon 487 (P-ala, P-thr, V-leu, V-val, V-pro). Results: We identified 54 EBNA1 sequences in the Canadian cohort and 10 sequences from Australia and USA. Twenty-one were from solid organ transplants (SOT) recipients of which 11 developed PTLD. There were 13 patients who had bone marrow transplantation (BMT) of which 3 developed PTLD. The transplant patient samples were compared to 10 IM samples (patients < 24 years of age). The predominant EBNA1 subtypes were: Canada - BMT, P-thr, 84.6%; Canada - SOT, P-thr, 71.4%; Canada - IM, P-thr, 80%; Australia, P-thr, 75%; USA, V-leu, 100%. The majority of sequences fell into two main clades. The strains from Canada clustered along with external strains with no clear evidence of geographic correlation. We identified EBNA-1 subtypes that were linked with specific mutation patterns that affect immune function. Conclusion: The dynamic phylogenetic tree enabled emerging PTLD strains to be defined in relation to existing strains from different patient groups.These strains were phylogenetically related to strains from geographic regions outside of Canada.

DraftModeStatus: 0

ID: 129
Defining Quality criteria for successful organ donation programs: A Scoping Review

Member of: CDTRP

Abstract Type: General Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Organ donation programs have been predominantly evaluated through benchmarking high-performance countries and the analysis of local quality indicators. However, to date, no definition of success in organ donation programs is available. Therefore, this scoping review aimed to synthesize the current evidence on key organizational attributes and processes of international organ donation programs associated with successful outcomes. Methods: Joanna Briggs Institute methodology for conducting scoping reviews was employed. The following databases were searched: PubMed, CINAHL, Embase, LILACS, ABI Business ProQuest, Business Source Premierand grey literature (Organ donation association websites, Google Scholar - first eight pages). To supplement the above, searches for gray literature were performed, and relevant websites were perused. Results:84 articles were included. These originated mostly from USA (n=33, 39.3%) and Spain (n=17, 20.2%). Most articles were published in 2001-2010 (n=33, 39.3%) and 2011-2019 (n=59, 46.4%), with predominant quantitative approach (n=46, 54.8%), followed by opinion papers (n=12,14.3%), and reports (n=10, 11.9%). Qualitative analysis revealed 16 categories that were described as positively influencing success/effectiveness of organ donation programs (table 1). The categories were classified into three main components of successful organ donation programs: context (any social interaction, situations, or support documents within organ donation context that might have an impact (positive or negative) in organ donation programs' results), process (necessary steps/procedures and behavioural patterns to ensure effective and smooth donations), and structural (the pieces that tie organ donation programs together and ensure an optimal organ donation performance). Conclusion: Organ donation programs are complex and depend on multiple actions to their success. Therefore, success in organ donation should be thought by considering a balance between context, process and structural elements. The results of this scoping review will better inform future studies to have a more holistic view while evaluating organ donation programs.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/129_AbstractImage1_0603094227.pdf

DraftModeStatus: 0

ID: 131
Understanding the Influence of Inter-Professional Relational Networks within Organ Donation Programs in Ontario

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Member of: CDTRP

Abstract Type: General Abstract

Member Type: AHP

Science Type: Clinical Science

Group Category: Donation

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background:To optimize organ donation performance the nature and impact of complex factors need to be understood. Some factors are well known and might not be modifiable (contra-indications for transplant, age limit of organ donor, etc.), but others (collaboration and communication) that contribute to variations among similar hospitals in the same province, are poorly understood. Thus, the overall aim of this research is to understand the nature and impact of relationships within the organizational context of organ donation programs in Ontario. Methods:Multimethod exploratory, prospective study: (1) to describe the characteristics of social networks of health care professionals of the organ donation programs based on communication patterns (Social Network Analysis) and (2) to describe the organizational attributes and processes of on organ donation programs (Multiple Case-Study), and (3) to compare the influence of social networks and organizational attributes on the performance of organ donation programs (Network Comparison). The study sites include Ontario hospitals designated as type A based on trauma centre level (Public Hospitals Act classification) partners of the Ontario's Organ Procurement Organization. We finished data collection at site 1 and are in the process of recruiting 2 other sites. Results:the researcher observed three organ donation cases (2 DCDs and 1 NDD) at site 1 and mapped the communication network during those cases (figures 1, 2 and 3). More detailed analysis of site 1 data, as well as continuous data collection/analysis of other sites are being conducted and final results will be presented at the 2019 Canadian Transplant Summit. Conclusion:Identifying the characteristics of effective collaboration and communication patterns during the organ donation process will allow for the development of interventions within hospitals to facilitate better performance outcomes. Improvements within organ donation programs are important for all involved in organ donation, including patients and families, and health care providers.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/131_AbstractImage1_0603110112.pdf

Abstract Image 2: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12575/131_AbstractImage2_0603110113.pdf

Abstract Image 3: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12578/131_AbstractImage3_0603110113.pdf

DraftModeStatus: 0

ID: 132
FESABILITY OF A NATIONAL NGS PROGRAM FOR HLA EPITOPE MATCHING: A CANADIAN PERSPECTIVE

Member of: CST

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Aim: Implementation of a national epitope-based matching requires high-resolution sequence information for all transplant recipients and donors. We have conducted a comprehensive health technology assessment of NGS to support the operational needs of Canadian programs within a national framework. Methods: We have examined technologies, chemistries and bioinformatics, platforms for NGS in over 5,000 subjects from a diagnostic laboratory perspective comprising analytical precision, implementation (training, operation, support) and economic criteria. Results: Our evaluation shows that short-range sequencing or long-range sequencing using nanopore technologies each offer specific advantages and challenges. To streamline implementation for Canadian laboratories we have first adopted the former. Technology advantages for a national program include: (a) advances in chemistry which have dramatically improved precision, with a drop-out rate reduced to 1% primarily at DQB1*03:01/02 and DRB4*01:01 in 1,000 patient sequences; (b) parallel multi-stream operation that enable rapid reporting of up to 5,000 samples / year; (c) standardized programs enable rapid training and certification of experienced HLA technologists in sequencing and analysis within approximately 4 weeks, and (d) economic costs of NGS sequencing of all 11 HLA genes compare favorably with SSO ($300 vs $357). Technology disadvantages include: (a) acquisition costs of new technology; (b) complex IT requirements for systems support, connectivity and security, (c) important data storage demands (6 gb/run, 8 gb processed data, raw data if required) and (d) inability to perform sequencing for urgent samples including deceased donors. Conclusion: NGS is ideally adapted to provide rapid, reliable and cost-efficient patient sequence data for epitope-based matching in high-throughput laboratories, but alternative molecular methods are still currently required for deceased donor typing.

DraftModeStatus: 0

ID: 133
Whole blood versus packed red blood cell-based perfusate in kidney normothermic machine perfusion

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Kidney transplantation is the gold standard treatment for end-stage renal disease, however an increasing gap between supply and demand has driven increasing interest in using marginal donor grafts. Normothermic machine perfusion (NMP) is a novel organ preservation method that offers opportunities for marginal kidney graft evaluation and therapeutic interventions not possible with traditional hypothermic methods. With a higher metabolic demand, NMP requires an oxygen carrier for efficient tissue oxygenation, and the most common choice is packed red blood cells or leukocyte depleted blood. We aim to investigate the effects of whole blood compared to packed red blood cell-based NMP perfusate on graft inflammation and perfusion. Methods: Porcine kidneys are recovered and perfused with our pressure controlled NMP system for 12 hours. The NMP system is primed with 300ml or 450ml (for packed red blood cell) of a modified plasmalyte crystalloid solution and either 300ml whole donor blood or 150ml packed red blood cell. Perfusate is supplemented with heparin, glucose, and insulin over time through infusions. Results: Both groups experienced comparable mean renal blood flow consistently over 12 hours of perfusion, with a trend showing increased renal blood flow in whole blood perfusates (whole blood: 719+27.5ml/min; packed red blood cell: 639+28.8ml/min). No significant differences in perfusate pH were detected. Cytokines TNF-alpha, IL-6, and IL-10 were significantly increased in whole blood compared against packed red blood cell-based perfusate. Conclusion: Both whole blood and packed red blood cell-based perfusates demonstrated equivalent perfusion resistance and perfusate biochemistry in a porcine model of kidney normothermic machine perfusion. With the presence of leukocytes in whole blood-based perfusates, there was a significant increase in perfusate cytokines, including both pro-inflammatory cytokines TNF-alpha and IL-6 and anti-inflammatory cytokine IL-10. However, the physiological significance of perfusate cytokine presence still requires further study through histological evaluation and a transplant model with long term follow up.

DraftModeStatus: 0

ID: 134
LOSS OF HETEROZYGOSITY OF HLA GENES IN HEMATOLOGICAL MALIGNANCIES: RECOMMENDATIONS FOR PREVENTING HLA MISASSIGNMENTS

Member of: CST

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Background: Loss of heterozygosity (LOH) is a well recognized genetic abnormality in hematological malignancies and when involving the HLA genes on Chromosome 6, can result in erroneous HLA typing. LOH is most frequently observed during blast crises pre-transplant occurring in 3-4% of patients with Acute Myeloid Leukemia (AML) (Dubois et al., 2012), and up to 12% in acquired Aplastic Anaemia (aAA) (Heyrman et al., 2017). Methods: Full HLA-11-Loci gene sequencing was established in Oct 2016 for the BC bone marrow program. Since then 2000 patients and donors have been fully typed using NGS. Samples were assessed for relative buffy coat volume, as well as CBC. Diagnosis information for high risk patients (AML) and a large buffy coat resulted in the sample being flagged for evaluation. Results: Out of the 2000 patients sequenced by NGS we have observed two cases of LOH, one of an entire haplotype and one of a single HLA gene (HLA-C). In both cases, NGS detected only 1 allele/haplotype in the pre-transplant blood sample, but was able to detect a 2nd allele/haplotype using a saliva sample. Conclusions: Several factors should be taken into account when genotyping HSCT patients, in order to prevent HLA mis-assignments: (a) Sample timing: disease state impacts timing of confirmatory typing. Pre-transplant patients in crisis are more likely to have clonal amplification of the mutated clone. (b) Sample type: Using buccal or saliva samples rather than blood at time of diagnosis, or remission blood samples limits the possibility of sampling the tumor. (c) Disease type: Whilst LOH has been reported in multiple diseases, certain diagnoses are more at risk for LOH. (d) Abnormal leukocytosis associated with high tumor burden is a risk factor for LOH. (e) Reflex testing of homozygous HLA results should be confirmed with at least two different methods with different sensitivities.

DraftModeStatus: 0

ID: 135
Human leukocyte antigen (HLA) class II expression on thymic regulatory T cells (Tregs) is induced by expansion conditions

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Associate

Science Type: Basic Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: BACKGROUND: Immune-modulating Tregs are a promising therapeutic tool in transplantation. Abundant Tregs can be isolated and expanded from discarded human thymuses (Dijke et al., AJT, 2016), indicating potential of thymic Tregs as an 'off-the-shelf' cell therapy. HLA upregulation on activated Tregs may increase their immunogenicity, which is a possible obstacle for clinical purpose. Here, we studied HLA class II expression on thymic Tregs under various expansion conditions. METHODS: FOXP3+CD25+ Tregs isolated from infant thymuses (n=5) by mechanical dissociation and magnetic-bead-based cell separation were cultured under various conditions for 14 days (TABLE 1). Additionally, anti-IFN-γ antibodies were added to condition B to study the role of IFN-γ. Treg phenotype and HLA class II expression were assessed by flow cytometry. Cytokine production was analyzed by multiplex assay. Cytotoxicity assays were done using anti-HLA class II antibodies and rabbit complement. RESULTS: Before culture, < 6 % of thymic Tregs expressed HLA class II. Treg expansion was observed in all culture conditions, except condition H. Cultures with artificial antigen-presenting cells (conditions A, B, C, D) contained fewer HLA class II-expressing Tregs than T Cell Activator cultures (conditions E, F, G) [range: 2-45% vs. 18-84%, respectively; p < 0 .001]. Additionally, CST OpTmizer medium (conditions C, D) induced less class II-expressing Tregs than ImmunoCult-XF medium (conditions A, B) [range: 2-29% vs. 17-45%, respectively; p=0.004]. Addition of rapamycin had no effect. HLA class II+ Tregs were susceptible to antibody-dependent complement-mediated cell death. The percentage of class II+ Tregs was positively correlated to IFN-γ production (p=0.02) and decreased in the presence of anti-IFN-γ antibodies in a dose-dependent manner. CONCLUSION: The conditions used for Treg expansion affected the percentage of thymic Tregs that upregulate HLA class II, which at least in part was due to IFN-γ production by the cells. Expansion protocols that limit IFN-γ production may therefore generate less immunogenic therapeutic Tregs.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/135_AbstractImage1_0603031654.pdf

DraftModeStatus: 0

ID: 136
COMPARISON OF HLA ANTIBODY ASSIGNMENTS BETWEEN TWO LUMINEX-BASED PLATFORMS

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background:Given evidence that donor specific antibodies (DSA) to Human Leukocyte Antigens (HLA) adversely affect kidney transplant outcome, sensitive techniques for detecting HLA antibodies have been developed. Single antigen bead (SAB) Luminex-based tests, in particular, are highly sensitive and are used to define 'unacceptable' donor antigens in a virtual crossmatch. Although it has largely revolutionized HLA antibody detection, Luminex SAB assay however does present with some problems such as interfering substances and non-specific reactivity which can make interpretation challenging. Since the more unacceptable anti-HLA antibodies that a patient has decreases the pool of suitable donors and increases waitlist time, the correct assignment of anti-HLA antibodies is critical. The aim of this study was to investigate the concordance between two SAB assays manufactured by One Lambda and Immucor. Methods:The negative and positive correlations of antibody assignments for each bead with an identical HLA antigen, based on the Canadian national cut-off of 1000 MFI for One Lambda and the vendor recommended positive assignments made by Immucor, were assessed for 50 patient sera. Alluvial diagrams were also generated to help with visualization of epitope patterns. Results: The positive correlation between the kits ranged from 70-80% depending on the locus and the negative assignment correlation was generally over 90%. LOG-MFI values were also compared between the 2 platforms for Class I and Class II beads combined and by Class, and the regression was comparatively modest (r2 = 0.63, 0.63,0.67), with the One Lambda kit having higher MFI values in general likely due to a higher serum to bead ratio. Conclusion: Although the two kits showed some correlation, there was also a significant amount of non-concordance.

DraftModeStatus: 0

ID: 137
Does thymoglobulin induction therapy reduce rates of delayed graft function in DCD kidney transplant recipients?

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: As the rate of delayed graft function (DGF) is high in donation after cardiac death (DCD) renal transplantation, some transplant physicians prefer to utilize Thymoglobulin (and delayed introduction of calcineurin inhibitors) over Basiliximab in order to reduce the rate of DGF. The purpose of this study was to compare the rates of DGF, rejection and survival of patients treated with either induction agent. Methods: A retrospective cohort study of recipients of 221 DCD kidney transplant recipients was performed between 2006 and 2018. Patient cohorts were stratified by induction agent. Calcineurin inhibitors were delayed in Thymoglobulin-treated recipients, but calcineurin inhibitors were not delayed with Basiliximab induction. The choice of induction agent was according to nephrologist preference. Demographic data in addition to immunologic risk based upon %PRA was collected. The primary outcome was DGF, defined as requiring dialysis within 7 days of transplant. Secondary outcomes included acute rejection, graft failure and survival. Student's t-test and Chi-square were used for statistical analysis. Results: After a mean follow-up of 6.2 years, 46 were induced with Basiliximab and 175 were induced with Thymoglobulin. Donor and recipient demographics were similar between groups. In fact, the mean %PRA was 26% in the Basiliximab group and 32% in the Thymoglobulin group (p =0.23). The rate of DGF was 55.6% in the Basiliximab group compared with 58.3% in the Thymoglobulin group (p=0.55). As well, acute rejection rates (15% both groups), 1 year creatinine clearance (77.6 ml/min and 73.7 mL/min in Basiliximab and Thymoglobulin group) and graft failure rates were similar between the groups (------p=------0.85, p=0.88). Conclusions: The use of Thymoglobulin and delayed introduction of calcineurin inhibitors did not reduce DGF rates, nor the risk of acute rejection or graft failure. Basiliximab is efficacious as an induction agent in the low immunologic risk DCD renal transplant recipient.

DraftModeStatus: 0

ID: 138
A Fortunate Problem: Allocating Non-Directed Living Donor Livers

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Member of: CDTRP

Abstract Type: Adult Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background Living liver donation is an accepted way of addressing patients' needs amidst a scarcity of usable deceased-donor livers. As with other procedures entailing medical risk, voluntary informed consent is crucial. Our transplant program is fortunate enough to receive offers from time to time from individuals who wish to donate part of their liver to a complete stranger. In contrast to anonymous non-directed living donor (ANLD) kidneys, which are allocated algorithmically as though they were deceased donor organs, ANLD liver donation poses an allocation quandary. Patients who are next in line for a deceased donor liver are typically not considered suitable candidates for a living donor transplant, as they generally need a whole liver. If the established allocation system, based on disease acuity as reflected in MELD scores, is not an appropriate or useful guide, how shall we allocate ANLD livers? We address this gap in the existing literature by laying out ethical and practical considerations bearing on the allocation of ANLD livers. Methods Surveying the literature on the ethics of organ allocation and donor and recipient outcomes, we identify a set of applicable moral considerations including donor factors, recipient characteristics, and public expectations. We then propose an iterative process for narrowing the pool of plausible recipients to one or two ideal candidates (i.e. a recipient and "backup"). Results and Conclusion A strong case can be made for matching ANLD offers first with smaller recipients on the basis of minimizing donor risk by minimizing the volume of liver to be transplanted. Among plausible candidates, priority may defensibly be given to patients who are reasonably likely to have good transplant outcomes and are thought to be disadvantaged under existing rules for allocating deceased-donor livers. The propriety of preferring younger candidates or those who have made reasonable efforts to find a living donor remains debatable.

DraftModeStatus: 0

ID: 139
Half a Chance: Extending Split Liver Transplantation in North America

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Member of: CDTRP

Abstract Type: General Abstract

Member Type: Associate

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background The human liver's ability to regenerate presents unique opportunities for some patients in need of transplant to derive long-term benefit from less than a whole liver. Notably, deceased donor livers may be split to benefit two different recipients. This presentation examines the ethical and practical implications of split liver transplantation (SLT) from deceased donors. After elucidating the ethical permissibility of this practice, the presenters will identify and assess potential mechanisms for expanding access to SLT in controlled conditions. Methods A review of the relevant literature shows that two normative considerations loom large over organ allocation policy: expected medical outcomes and equitable access. We critically appraise how SLT aligns with these objectives in light of present surgical capabilities. Insofar as SLT remains rare, we draw on our knowledge of the structure of organ allocation and culture of surgery to theorize why this is the case. Finally, we consider how allocation mechanisms and variances employed in other "special situations," might be adapted to better facilitate SLT. Results and Conclusion The impact of SLT on individual and aggregate patient outcomes is an empirical question that turns on factors such as selection criteria. Nonetheless, studies strongly suggest that SLT can increase the total number of recipients benefiting from transplantation. While the equitable analysis is also complex, SLT may benefit hard-to-match recipients who are disadvantages through no fault of their own. Hence, in conditions of scarcity, SLT is ethically supportable. We propose that a major obstacle to greater splitting of deceased donor livers in North America is allocation infrastructure that was not designed with this possibility in mind. Potential mechanisms for advancing SLT including establishing a central clearinghouse for identifying livers suitable for splitting and offering them first on this basis, as well as a separate registry for evaluating and monitoring SLT outcomes.

DraftModeStatus: 0

ID: 140
The impact of delayed graft function on DCD renal transplant outcomes

Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Delayed graft function (DGF) is associated with inferior outcomes in donation after neurologic death renal transplantation. As a result of warm ischemic time, DGF occurs far more often following donation after circulatory death (DCD) transplantation, but it's effect on outcomes are unclear. We sought to examine the impact of DGF on DCD kidney transplants. Methods: Demographics and outcomes of 201 DCD kidney transplant recipients were assessed at a single institution between 2006 and 2018. Cohorts were classified as having immediate graft function (IGF), or DGF(requiring dialysis within 7 days of transplant). We further subclassified groups into short and prolonged DGF (defined as DGF lasting longer than 7 days). The primary outcome was graft survival and secondary outcomes included 1 year creatinine clearance, rejection and overall survival. Results: Overall, 58% of DCD renal transplants experienced DGF. Donor and recipient demographics were similar between IGF and DGF groups. The presence of DGF did not affect patient or graft survival after a mean of 7.2 years (1-12 years) (Figure 1). Although the presence of DGF affected CrCl at 1 ($p < 0.0001$, 95% confidence interval 14.5 – 30.8), and 3 months ($p < 0.003$, 95% confidence interval 4.5 – 21.7), 1 year CrCl was not different in the group with DGF vs. IGF ($p = NS$). Although DGF increased the duration of admission, it did not affect re-admission rates ($X2 = 1.04$, $p = 0.31$). DGF was associated with a higher acute cellular rejection rate ($X2 = 1.04$, $p = 0.31$). Interestingly, graft survival was inferior in patients with prolonged DGF, but this small subgroup was associated with a high rate of rejection. Conclusion: In the setting of DCD renal transplantation, the presence of DGF had no impact on graft or patient survival. Although prolonged DGF is associated with inferior graft outcomes, this appears to be associated with graft rejection.

Abstract Image 1:

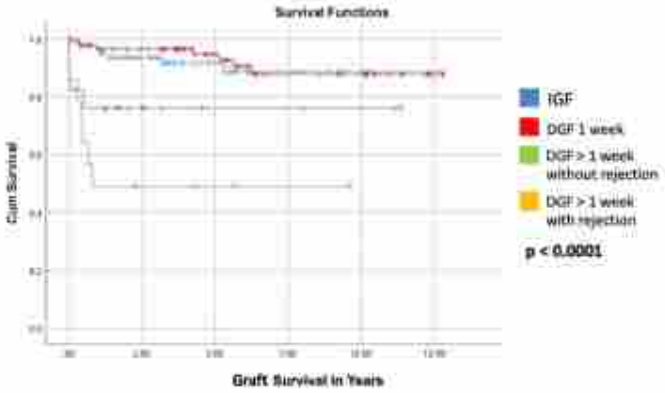

Fig 1. Graft survival was not different between IGF, DGF and prolonged DGF without rejection, but worse in prolonged DGF with rejection ($p < 0.0001$).

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DraftModeStatus: 0

ID: 141
Pushing the beans to the brink: longer functional warm ischemic time confers acceptable outcomes of DCD kidney transplant

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Member of: CST

Abstract Type: Adult Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Kidney-Pancreas

Submission: Oral or Poster/E-Poster

Trainee: No

Abstract Body: Background: Donation after cardiac death (DCD) increases the donor supply of transplantable kidneys, however prolonged agonal and warm ischemic phases can be deleterious to graft function, potentially compromising outcomes. We sought to better define the impact of prolonged functional warm ischemic time (agonal time at MAP = 30 minutes (WIT2). Demographic data as well as graft functional outcomes were collected and reviewed and compared between cohorts using t-test and Chi-square. Kaplan-Meier survival analysis was utilized to compare graft survival according to cohort. Results: A total of 201 DCD kidneys were included in analysis, with 151 in WIT1 (median 19 mins, IQR 16.0-22.5) and 50 in WIT2 (median 37 mins, IQR 31.0-45.8). Mean age, BMI, age of donor/recipient, gender distribution, anastomosis time, and cold ischemic time did not differ between the groups. The number of expanded criteria donor kidneys were 32 (21.2%) and 6 (12%) in WIT1 and WIT2, respectively, with no difference. Figure 1 shows that there were no difference in graft survival between groups (p=0.43). The mean Creatinine at 1 year was 153.5 umol/L and 162.7 umol/L in WIT1 and WIT2, respectively (p=0.40). The incidence of DGF and rejection did not differ between the two groups. Conclusions: Although we believe that fWIT is an important variable in DCD kidney graft outcomes, fWITs around 30 min are acceptable for donation. With experience of greater number of fWITs beyond 30 min, we may eventually determine a fWIT duration at which time DCD kidneys need to be discarded.

Abstract Image 1:

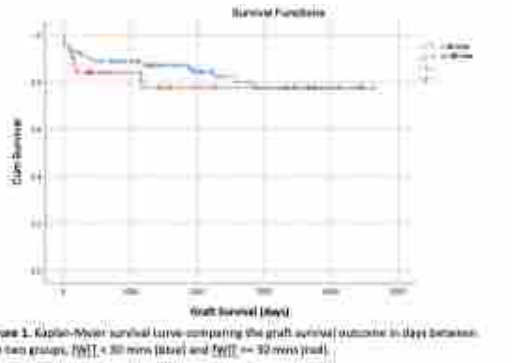

Figure 1. Kaplan-Meier survival curve comparing the graft survival outcome in days between the two groups, fWIT < 30 mins (blue) and fWIT >= 30 mins (red).

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DraftModeStatus: 0

ID: 142
Determining the role of von Willebrand Factor in potential thrombotic complications that are associated with aging and organ transplantation

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Member of: CST

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: von Willebrand factor (VWF) is a pro-coagulant glycoprotein expressed only in endothelial cells and megakaryocytes. It mediates adhesion of platelets to the endothelium/sub-endothelium. External stimuli, including aging and hypoxia can upregulate VWF. Increased production of VWF, is a significant risk factor for thrombus formation. We are investigating whether conditions such as aging and transplantation, which exposes the donor organs to hypoxia, can affect expression pattern of VWF. Objectives: To determine whether increased VWF levels that we observe in the aged and donor organs are accompanied by alterations in VWF vascular expression pattern; and whether this corresponds to increased thrombogenicity. Methods: Procured pig's lungs that are maintained in cold storage or exposed to warm perfusion (before and after perfusion), as well as harvested major organs of aged and young mice will be subjected to immunofluorescent analysis to investigate vascular expression pattern of VWF in small compared to large vessels. Also, similar analyses will perform in organs of aged compared to young mice, but additionally determine the presence of platelets aggregate formation in these mice organs. Results: Analyses have demonstrated that VWF mRNA and protein levels are altered in an organ-specific manner in aged compared to young mice. We have also shown that VWF mRNA and protein levels are increased in lungs that are being processed for transplantation, depending on the pre-transplant storage conditions. Cold storage leading to increased VWF compared to warm perfusion suggestive of a role for hypoxia-induced upregulation of VWF in the lung vasculature. Conclusions: Results will reveal whether conditions that leads to VWF upregulation, including organ storage prior to transplantation, and aging, will induce (i) VWF alteration in expression pattern, and (ii) platelets aggregate formation and potentially thrombosis. The results will provide insights towards development of anti-thrombotic approaches that would be advantageous in transplant procedures and in aging population.

DraftModeStatus: 0

ID: 143
ABO tolerance following treatment of infant wild-type mice with A-expressing syngeneic erythrocytes

Member of: CDTRP

Abstract Type: General Abstract

Member Type: Full

Science Type: Basic Science

Group Category: Heart

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Background: ABO-incompatible heart transplantation (ABOi HTx) is safe in young children and increases donor access. Post-ABOi HTx, B cell tolerance develops to donor ABO blood group antigen(s) by mechanisms not fully defined. To study ABO tolerance, we developed A-transgenic mice (A-Tg) that express A-antigen on vascular endothelium, erythrocytes (RBCs) and lymphocytes; we demonstrated A-antigen-specific tolerance induced by HTx into 4-week-old, MHC-identical, wild-type mice. Intentional induction of tolerance may allow subsequent ABOi HTx. Recently, we showed ABO tolerance could be intentionally induced in wild-type mice after intraperitoneal (ip) injection of infant mice with intact A-Tg blood cells (BCs). Herein, we sought to determine specific A-Tg cell type(s) capable of inducing tolerance. Methods: Wild-type BALB/c (BALB) mice at 7 days of age were left untreated or injected ip (weekly×3) with either unfractionated BCs, RBCs, peripheral blood mononuclear cells (PBMCs), or splenocytes from A-Tg BALB mice (see Table). Two weeks later, all mice were injected ip (weekly×5) with human A-RBC (A-antigen challenge) in an attempt to elicit anti-A antibody production. Serum anti-A and third-party (non-A anti-human) antibody were assessed by hemagglutination or ABH glycan microarray. Results: In response to challenge with A-antigen, high levels of anti-A antibody were produced both in untreated mice and in mice previously treated with A-Tg PBMCs or splenocytes (Table). In contrast, anti-A antibody remained undetectable/very low in mice treated as infants with A-Tg BCs or RBCs. Third-party antibody responses were high for all groups. Conclusion: A-Tg RBCs induced robust A-antigen-specific tolerance in infant mice, whereas A-Tg lymphocytes (PBMCs, splenocytes) did not. Future studies will explore mechanisms of A-Tg RBC tolerance induction with the goal to design synthetic ABH-multivalent polyethylene glycol (PEG) glycoconjugates for intentional ABO tolerance to allow subsequent ABOi HTx safely.

Abstract Image 1:

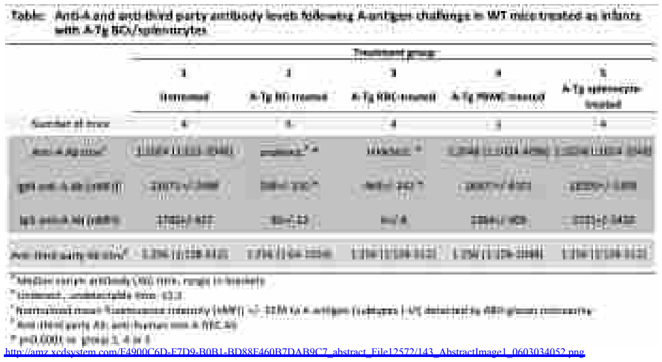

Table: Anti-A and anti-third party antibody levels following A-antigen challenge in WT mice treated as infants with A-Tg BCs/splenocytes

	Treatment group				
	1 Untreated	2 A-Tg BC-treated	3 A-Tg RBC-treated	4 A-Tg PBMC-treated	5 A-Tg splenocyte-treated
Number of mice	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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ID: 144
COMPARISON OF HLA ANTIBODY ASSIGNMENT BETWEEN TWO LUMINEX PLATFORMS IN A COHORT OF THORACIC PATIENTS

Member of: CST

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Aim: To evaluate and compare the reliability of HLA-antibody detection in thoracic patients using either LabScreen (OL) (One Lambda, USA) or LifeCodes (IM) (Immucor, USA) Single Antigen (SA) Luminex assays. Methods: Sera of heart or lung transplant patients were tested with OL and IM SA assays and analysis performed with OL Fusion and IM MatchIT software. A matrix of 147 beads was constructed to compare those with identical HLA antigen common to both assays using raw trimmed MRI values, two-tailed test, fixed effect B-spline modeling, and distribution analysis using SAS v9.4 software. Results: The study comprised 164 patients with paired testing, of whom 30 cardiopulmonary recipients are reported here. Clinically important and statistically significant differences were highlighted between the 2 assays for both class 1 and 2 reactivities (p (Figure 1). B-spline comparison shows that overall, OL values trend with a higher raw MFI value. Using different thresholds of MFI, distribution analysis shows that OL has higher variance lower thresholds relative to the IM assay, but better was correlation observed at a threshold of >2000 (Fig 1b). The area of uncertainty was greatest for alleles with marginal values, though discrepancy also occurred at those with higher values in the OL assay. Conclusions: There is a poor correlation between the 2 assays particularly at marginal MFI values which is concerning since incorrect assignment decreases the pool of potential donors and increases waitlist times.

Abstract Image 1: http://amz.xcdsystem.com/F4900C6D-F7D9-B0B1-BD88F460B7DAB9C7_abstract_File12572/144_AbstractImage1_0603035949.gif

DraftModeStatus: 0

ID: 145
EVALUATION OF BUCCAL SWABS FOR CONFIRMATORY RECEPIENT DNA AND DONOR INITIAL SCREENING IN BC BONE MARROW PROGRAM

Member of: CST

Abstract Type: General Abstract

Member Type: Full

Science Type: Clinical Science

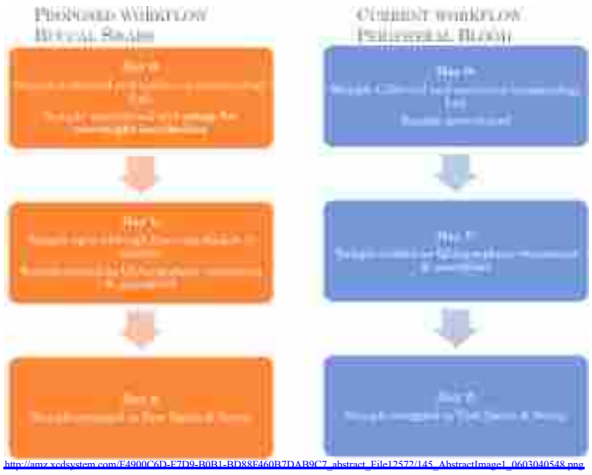
Group Category: Other

Submission: Poster/E-Poster only

Trainee: No

Abstract Body: Aim: A switch from blood to buccal swab for confirmatory typing of hematopoietic stem cell transplant (HSCT) has been driven by the increased ease of sample collection (both locally and internationally) and patient comfort and the issue of observed loss of heterozygosity (LOH) in BMT patients. Buccal DNA collected at a second time point meets ASHI requirements as a second sample source and would meet all our requirements to provide the bone marrow program with a viable option for collecting both potential BM donors and recipients. Methods: We assessed 6 collection kits, including wet and dry swabs from a variety of vendors. Recapitulating real-life scenarios for the laboratory, multiple time points post-collection (0, 24, 48, 72hr) with samples stored at room temperature from self-administered collections. Different automated extraction protocols for the QiaSymphony were evaluated, in conjunction with various pre-treatment protocols to optimize DNA quality and quantity. All samples were typed by SSO (OneLamdba) and NGS sequencing (Omixon Holotype) for comparison purposes. Results: Our evaluation showed that a number of vendor kits were not suitable for HLA typing, due to poor yield or consistent failure of a single locus. Having selected the Puritan™ TT collection kit, pre-treatment protocols of 16hr incubation with proteinase K followed by the QiaSymphony Mini Kit with Tissue_LC_200_v7_DSP protocol resulted in consistently higher yields of DNA (~9-20ng/ul). SSO typing for DRB1 and NGS typing for DQB1 and DPB1 were the most susceptible to failure. Conclusion: Using buccal swab-extracted DNA with the outlined processing protocol provides a valid method capable of accurate test results for HSCT patients. In addition, the use of buccal samples provides a biological specimen which is less likely to be susceptible to LOH for HSC transplant patients who were initially typed by peripheral blood extracted DNA.

Abstract Image 1:



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DraftModeStatus: 0

ID: 146
Distinction between Hepatorenal Syndrome and Non-Hepatorenal Syndrome Acute Kidney Injury has no Impact on Renal Function Recovery Post Liver Transplantation

Member of: CST

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

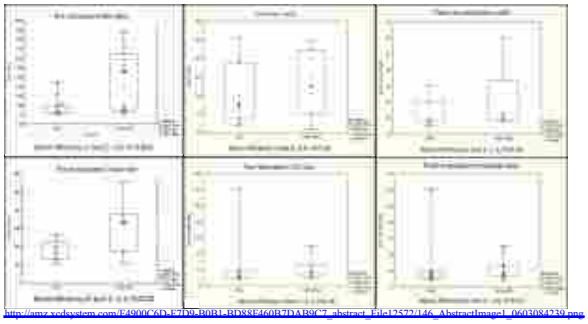
Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Acute Kidney Injury (AKI) in cirrhosis is often further categorized into Hepatorenal Syndrome (HRS) vs non-HRS to predict renal recovery post-transplant. This distinction is often cumbersome due to overlapping causes of AKI and ever-changing criteria of HRS. We here review the patterns of renal recovery after liver transplantation to reassess the relevance of this distinction. Methods We retrospectively analysed recovery of renal function after liver transplant. We assessed the difference in intensive care unit stay, hospital stay, nadir creatinine, and time to achieve nadir in patients with or without HRS. Results: 90 patients who underwent liver transplantation were reviewed, of whom 32 had acute kidney injury. We excluded patients who were transplanted for acute liver failure, polycystic liver disease, urea cycle defects, those who had a prior liver or kidney transplant, and those who did not survive till discharge. 25 patients were considered for final assessment. Median age of patients was 60(IQR 56-63), and 64% were males. Median MELD score was 25(IQR 17-33). Alcohol was the most common etiology(40%) followed by viral and NASH(24% each). Median creatinine at the time of transplant was 172 mmol/L(IQR 144-262). All patients had current or past ascites. HRS was considered the cause of AKI in 14(56%) cases. Time to achieve creatinine nadir and ICU stay both correlated strongly with pre-transplant bilirubin (r=0.71, 0.51 respectively) and modestly with post-transplant creatinine peak(r=0.43, 0.40 respectively) but not with pre-transplant creatinine. The HRS group showed significantly lower bilirubin (28 vs 444 mmol/L, Z=-2.8, p=0.006) and creatinine (163 vs 323 mmol/L, Z=-2.2, p=0.02), however, there was no difference in peak creatinine post-transplant, nadir creatinine, time to achieve nadir, ICU stay, or overall hospital stay. Conclusion: Distinction between HRS and non-HRS AKI may play a major role in prognosticating renal recovery on patients with decompensated cirrhosis undergoing liver transplant

Abstract Image 1:



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DraftModeStatus: 0

ID: 147
Serial monitoring of the alloreactive T cell compartment in lung transplant recipients

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Member of: Student/Others

Abstract Type: General Abstract

Member Type: Trainee

Science Type: Basic Science

Group Category: Lung

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: Measurement of T cell alloreactivity may facilitate a more accurate prediction of graft outcome and the optimization of immunosuppression. We have developed a high-throughput immune synapse detection (ISD) method using imaging flow cytometry to define the composition and size of the alloreactive T cell repertoire in healthy donors. We hypothesize that ISD can be used to predict lung allograft outcome. Furthermore, we are using longitudinal post-transplant blood samples to examine the association of T cell alloreactivity – as measured by ISD – with clinical acute rejection. Method: We have prospectively collected blood samples from 50 donor and recipient pairs of lung transplant cases. Monocyte-derived dendritic cells from donors and recipients were produced and cryopreserved. In addition to pre-transplant, T cells from 3-, 6-, 9-, and 12-months post-transplant have been isolated. T cells and DCs are co-cultured for 4 hours prior to fixation and staining in advance of ISD on an ImageStream Mark X imaging flow cytometer. Results: Donor monocyte-derived dendritic cells had relatively uniform MHC class II and costimulatory molecule expression, making them suitable for use in ISD. In an initial set of 5 patients, T cell immune synapse frequency generally increased post-transplant compared to pre-transplant values, with significant variations over time post-transplant. The majority of alloreactive immune synapses in lung transplant recipients were made by memory CD4+ T cells. Further analysis in the remainder of the cohort is now underway. Conclusion: We have collected donor antigen-presenting cells and recipient T cells from a cohort of lung transplant recipients and have demonstrated the feasibility of measuring alloreactivity in these patients using ISD. Further work will examine the association of ISD results with clinically relevant endpoints including acute rejection, humoral sensitization, and allograft dysfunction.

DraftModeStatus: 0

ID: 148
Splenectomy is associated with higher rate of late rejection in post liver transplant (LT)

Member of: Student/Others

Abstract Type: Adult Abstract

Member Type: Trainee

Science Type: Clinical Science

Group Category: Liver

Submission: Oral or Poster/E-Poster

Trainee: Yes

Abstract Body: Background: In LT recipients, splenectomy is occasionally performed for various reasons including thrombocytopenia, ABO incompatibility and small for size syndrome. Splenectomy may influence immunological reactions and influences the rate, type and severity of post liver transplant rejection. We studied the effect of splenectomy on rejection pattern after LT. Methods: Between January 2012 – December 2016, 788 adult LT were performed in our program. 30 recipients had splenectomy prior or at the time of LT. Recipients were matched 1:2 based on age, MELD and platelets at the time of LT, presence of HCC and type of LT to recipients without splenectomy. Time interval to rejection {early(6 months)}, number of rejection episodes and type of rejection (acute vs chronic) were analyzed between the groups. Results: 14 (46.6%) LT recipients in the splenectomy group had at least one episode of rejection post LT compared to 191 (25.2%) in non-splenectomy group (p=0.35). Average time to first rejection was longer for splenectomy patients (257.7 days) than non-splenectomy patients (150.73 days) (p=0.36). There were a total of 13 early rejections in the splenectomy group compared to 168 early rejections in the non-splenectomy group (p=0.78). All were acute cellular rejection and responded to treatment. In contrast, late rejection was seen in 4 (13.33%) splenectomy recipients which is significantly more frequent compared to 52 (6.86%) non-splenectomy recipients (p=0.02). In multivariate analysis, splenectomy, use of basiliximab, higher platelet transfusion during transplant surgery , and bilirubin on day 1 post LT were significantly associated with higher likelihood of late rejection. In contrast, tacrolimus based immunosuppression , BMI, creatinine at 1 month post LT were inversely related to likelihood of late rejection. (Table 1) Conclusion: Our study shows that splenectomy was associated with higher likelihood of late rejection (>6 months after LT) in post LT recipients.

Abstract Image 1:

Table 1 showing variables for late rejection (> 6 months post LT)

	OR	Standard Error	p Value	95% CI
Splenectomy	12.09	19.48	0.02	1.31 – 110.8
Basiliximab Induction	9.35	05.87	3.88	2.73 – 32.00
Use of platelets during LT	1.43	0.140	0.00	1.17 – 1.75
Bilirubin 1-day post LT	1.00	0.000	0.00	1.00 – 1.01
BMI at LT	0.85	0.060	0.00	0.74 – 0.98
Tacrolimus	0.20	0.150	0.03	0.06 – 0.87
Creatinine 1-month post LT	0.57	0.094	0.00	0.41 – 0.75

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DraftModeStatus: 0

ID: 183
DCD Hearts: A possible medical legal and ethical framework

DraftModeStatus: 0

ID: 184
Education to Increase Pursuit of Transplant: State of the Field and New Innovations

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DraftModeStatus: 0

ID: 185
Molecular Phenotyping of Transbronchial and Mucosal Lung Transplant Biopsies: the INTERLUNG study

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