ALBERTA TRANSPLANT INSTITUTE

Research Day

2023

May 10

Register Here

With thanks to our Sponsors

astellas

paladin
une compagnie de endo international
an endo international company

Table of Contents

As we have immune-compromised individuals attending ATI RESEARCH DAY 2023, we are requiring masking at all times unless you are presenting. Thank you for wearing masks and protecting the very patients we are here to serve.

Message from the Director

Welcome to ATI Research Day 2023!

Dr. Lori West, OC, MD, DPhil, FRSC, FCAHS, FRCPC

This past year has been a year of revitalization, community engagement, and increasing momentum for the Alberta Transplant Institute (ATI). Our vision is that the ATI is a hub to lead the Alberta donation and transplantation ecosystem to excellence in research, education, and advocacy. To work towards this vision, we have spent the year focused on strengthening the Institute's foundations, including engaging our membership, nurturing partnerships, and highlighting the stellar work being done in Alberta across our pillars of research, education, and advocacy.

On the research front, one of our key priorities this year was to establish an effective mechanism to identify and prioritize the community's top research needs and connect research expertise across the Alberta donation and transplantation ecosystem. You can expect to hear more about the results of this process and get involved in the next steps at the Research Priorities Networking Roundtable session at Research Day at 9:45am. With shared priorities established, we are looking forward to developing ways to support ATI members to tackle the key research questions identified.

As you will see from the program and abstracts, the quality and breadth of the research ATI members are undertaking is inspiring. Our basic science and clinical researchers have submitted topics ranging from advances in ex vivo technologies to pharmaceuticals, and from basic immunology to transplant outcome research. A total of 27 abstracts were submitted and will be showcased over the course of the day through presentations and posters. I encourage everyone to capitalize on the opportunity to support trainees, build your network, and learn more about the wide range of donation and transplantation research happening in Alberta.

Looking forward to 2023-2024, we are very excited to build on these successes as we shift from ATI strategic research planning into action. Enhancing the connectivity of the donation and transplantation ecosystem and leading the community into the future requires broad collaboration. We are thrilled to continue building connections within and between our communities at Research Day 2023, and have no doubt that the excellence that will be showcased provides a strong foundation for our collective future success.

Program at a glance

May 10, 2023

08:00–08:15 Welcome (ECHA 1-420 and Zoom)
Dr. Lori West, ATI Director

08:15–09:15 Keynote: Dr. Alexandre Loupy (ECHA 1-420 and Zoom)
Moderator: Dr. Esme Dijke
Multidimensional Approaches in Solid Organ Transplantation: Insight for diagnostics and prognostics

09:15–09:45 Break

09:45-10:45 ATI Research Priorities Networking Roundtables
(ECHA 1-420/1-490 and Zoom)

10:45-11:00 Break

11:00-12:00 Poster Sessions
Virtual Poster Presentations begin at 11am in 1-420 and Zoom
In-person Posters begin at 11:15 in the hallway outside classrooms

12:00-13:00 Lunch break (takeaway lunch boxes)

13:00-14:00 Concurrent Selected Talks (ECHA 1-420/1-490 and Zoom)

14:00-14:15 Break

14:15-15:15 Patient, Family, and Donor Session (ECHA 1-420 and Zoom)
Bill 205 and Its Potential for Alberta

15:15-15:30 Break

15:30-16:15 Concurrent Professional Development Sessions
Breakout Room 1 (academic) : ECHA 1-420 and Zoom
Knowledge Mobilization: From Partnering and Planning to Proposals with Laura McAlpine
Breakout Room 2 (clinical): ECHA 1-490 and Zoom
Normothermic Regional Perfusion (NRP): Enabling Innovation while Preserving Healthcare and Public Trust with Drs. Charles Weijer and Marat Slessarev

16:15-16:30 Closing Remarks and Awards for Best Talk/Poster
(ECHA 1-420 and Zoom)

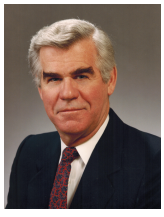
8:00 - 9:15 (ECHA 1-420 & Zoom)
Keynote Speaker: Dr. Alexandre Loupy

Alexandre Loupy, MD
Paris Translational Research
Center for Organ Transplantation
Paris Cité Université

Multidimensional Approaches in Solid Organ Transplantation: Insight for Diagnostics and Prognostics

Alexandre Loupy's research focuses on artificial intelligence and multi-organ transplantation analytics. It covers allograft transplantation, rejection, antibodies and population sciences. He has defended two PhDs, one in cell biology (2011) and the other in biostatistics (2014). Since 2015, he has been the head of the Paris Expertise Centre for Organ Transplantation in PARCC. In 2017 he was appointed Prof. of Nephrology and Epidemiology at Paris Cité Université in Paris, France. Prior to that, he was appointed Adjunct Professor at Cedars Sinaï, UCLA in Los Angeles, California. He has authored 310 publications, holds 5 patents and software protections, and has presented to over 32 international invited conferences since 2006.

Since 2015 he is appointed Scientific Director of the International Banff Classification Group and is also an expert for the FDA, a member of the American Society of Transplantation and is involved in the French Society of Transplantation and in the European Society of Transplantation. He is PI of on several national (RHU KTD-innov, iTRANSPLANT, Prix Emergence de la Ville de Paris, Prix Emergence en Recherche IdEX) and international grants (H2020 EU-TRAIN).



Supported by the William H. Lakey Transplantation Lectureship Fund

9:45-10:45 am (1-420, 1-490 & Zoom)
ATI Research Priorities Networking Roundtables

JOIN US IN CONVERSATION ABOUT THE ATI RESEARCH PRIORITIES PROJECT AND DISCUSS KEY PRIORITIES FOR THE NEXT 5-10 YEARS

Group 1:

Advance the Culture of Donation and Donation Practices - Living Donation
Leads: Ngan Lam (academic), Anne Halpin (living donor)

Group 2:

Advance the Culture of Donation and Donation Practices - Deceased Donation
Leads: Andreas Kramer (academic), Jennifer Woolfsmith & Boulet Family (donor families)

Group 3:

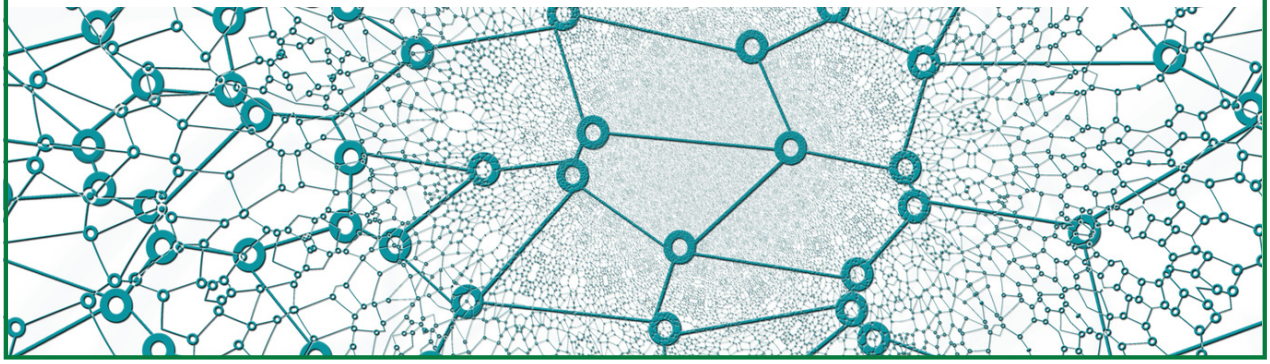
Optimize Graft Use and Quality
Leads: Kieran Halloran (academic), Murray Wilson (transplant recipient- In Memory)

Group 4:

Improve Immunologic Health for Transplant Patients
Leads: Esme Dijke (academic), Sean Delaney (transplant recipien)

Group 5:

Improve Long-term Wellness for Transplant Patients
Leads: Puneeta Tandon (academic), Lindsey Kemp (transplant mom)



1:00 to 2:00 pm (ECHA 1-420 and Zoom)
Concurrent Oral Presentations I (Moderator: Jason Acker)

1:00-1:15 pm - Presenter: Keir Forgie
"Negative Pressure Ventilation Ex-situ Lung Perfusion Successfully Preserves Porcine Lungs And Rejected Human Lungs For 36-hours"
Keir Forgie, Abeline Watkins, Katie Du, Alynne Ribano, Darren Freed, Jayan Nagendran

1:15-1:30 pm - Presenter: Nerea Cuesta-Gomez
"Small molecule AT7867 promotes pancreatic progenitor differentiation of human pluripotent stem cells for the treatment of diabetes"
Nerea Cuesta-Gomez, Kevin Verhoeff, Nidheesh Dadheech, Braulio Marfil-Garza, Ila Tewari Jasra, Rena Pawlick, Haide Razavy, AM James Shapiro

1:30-1:45 pm - Presenter: Jordan Wong
"Exploring local immune modulation with rapamycin-eluting microparticles to preserve islet graft function in mice"
Jordan Wong, Purushothaman Kuppan, Jessica Worton, Chelsea Castro, Karen Seeberger, Kateryna Polishevska, Joy Paramor, Gregory S Korbutt, Andrew R Pepper

1:45-2:00 pm - Presenter: Ibrahim Adam
"The role of sex and T cells in natural vs induced ABO antibody production in mice"
Ibrahim Adam, Bruce Motyka, Kesheng Tao, Lori West

1:00 to 2:00 pm (ECHA 1-490 and Zoom)
Concurrent Oral Presentations II (Moderator: Tony Kiang)

1:00-1:15 pm - Presenter: Aslak Kristoffersen
"Right ventricular dysfunction by echocardiography is an early marker of evolving Cardiac Allograft Vasculopathy in heart transplanted children"
Judith Namuyonga, Aslak Widerøe Kristoffersen, Nassiba Alami-Laroussi, David Youssef, Jennifer Conway, Michael Khoury, Lily Lin, Luke Eckersley, Nee Scze Khoo, Simon Urschel

1:15-1:30 pm - Presenter: Matthew Smith
"Statin Use in Liver Transplant: Indication, Use and Impact of Statins on Patient Outcomes"
Matthew K. Smith, Cora Laidlaw, Juan G. Abraldes, Rahima A. Bhanji

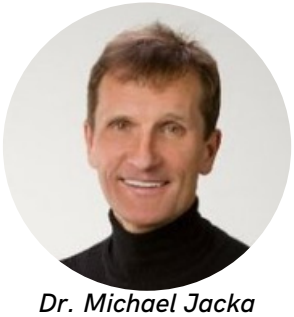
1:30-1:45 pm - Presenter: Kieran Halloran
"Molecular features of baseline lung allograft dysfunction"
Martina Mackova, Patrick Gauthier, Jessica Chang, Greg Snell, Glen Westall, Stephen Juvet, Jan Havlin, Phil Halloran, Kieran Halloran

1:45-2:00 pm - Presenter: Benjamin Adam
"DSA-Negative Microvascular Inflammation in Kidney Transplant Biopsies: Gene Expression Comparison with Native and Transplant Kidney Controls"
Anna Buxeda, Ivy Fixsen, Ian Gibson, Chris Wiebe, Peter Nickerson, Patricia Campbell, Julio Pascual, Marta Crespo, Michael Mengel, Benjamin Adam 1

2:15-3:15 pm (ECHA 1-420 & Zoom)
Patient-Family-Donor (PFD) Focused Session

Linda Powell, Chair of Alberta ORGANization Group

Jennifer Woolfsmith, AOG Member & Donor Mom



Dr. Michael Jacka Critical Care Physician

Dr. Anne Halpin, Moderator & Living Kidney Donor

BILL 205 AND ITS POTENTIAL FOR ALBERTA

Coming into force on April 1, 2023, Bill 205 (THE HUMAN TISSUE AND ORGAN DONATION (MANDATORY REFERRAL) AMENDMENT ACT, 2022) achieved a rare feat in modern politics: unanimous, all-party support from the Alberta Legislature on May 31, 2022. A key change resulting from this Act is enshrining 'mandatory referral' for potential organ and tissue donors into law.

This Session will feature key members of the Alberta ORGANization Group (AOG) and health providers involved in the donation system who have helped advise on this legislation from its inception through to implementation. They will discuss its potential for improving our overall organ and tissue donation and transplantation system in Alberta.

Audience members will be asked to be active participants in this panel discussion.

The day Bill 205 received Royal Assent at the Alberta Legislature (May 31, 2022). MLA RJ Sigurdson, members of the Alberta ORGANization Group, and other key patient/family partners

3:30-4:15 pm (ECHA 1-490 & Zoom)
Concurrent Professional Development Session I

Knowledge Mobilization: From Partnering and Planning to Proposals

Laura McAlpine
SPOR Project Coordinator
University of Alberta

In this session, Laura will provide an overview of knowledge mobilization - what it is and why it's important - and break down how to write about knowledge mobilization in grant proposals. She will focus on identifying impacted and influential groups, co-developing targeted and feasible plans, and demonstrating to grant reviewers that your team can carry out the long-term vision of the project.

3:30-4:15 pm (ECHA 1-420 & Zoom)
Concurrent Professional Development Session II

Normothermic Regional Perfusion (NRP) and Deceased Organ Donation: Enabling Innovation While Preserving Stakeholder and Public Trust

To increase the quality and number of organs available for transplant from deceased organ donors, a new perfusion technology, called Normothermic Regional Perfusion (NRP), circulates oxygenated blood through the abdomen or chest and abdomen of the deceased donor prior to organ retrieval. NRP is used routinely in Spain and a few other countries but not yet in Canada. While promising, NRP raises several ethical concerns. First, does NRP, which restores circulation to a region of the donor's body, invalidate the determination of death using circulatory criteria? Second, is NRP safe for the donor; that is, can we be sure that surgical safeguards prevent the restoration of circulation to the brain? Third, is specific consent to NRP required from donor families and, if so, how best to inform them? Only by carefully addressing these issues can we both enable innovation and preserve stakeholder trust in organ donation in Canada.

Charles Weijer &
Marat Slessarev
Western University

Abstracts - Oral Presentation

Negative Pressure Ventilation Ex-situ Lung Perfusion Successfully Preserves Porcine Lungs And Rejected Human Lungs For 36-hours

Keir Forgie[1,2], Abeline Watkins [2], Katie Du[2], Alynne Ribano [2], Darren Freed[3], Jayan Nagendran[1]

1. Cardiac Surgery, University of Alberta, Mazankowski Alberta Heart Institute, Edmonton, AB
2. University of Alberta, Edmonton, AB
3. Stollery Children's Hospital, Edmonton, AB

Purpose

Continuous Ex-Situ Lung Perfusion (ESLP) beyond 24-hours is required to optimize the extended criteria donor pool through cell- and gene-based therapies. Preclinically, continuous ESLP for 24-hours is the longest duration achieved in large animal models and rejected human lungs. We present the results of our 36-hour Negative Pressure Ventilation (NPV)-ESLP protocol applied to porcine and rejected human lungs.

Methods

Five sets of domestic pig lungs (45-55kg) underwent 36-hours of NPV-ESLP. Two sets of human lungs rejected for clinical transplant were donated to research and preserved on NPV-ESLP for 36-hours. Graft function was assessed via physiologic parameters, edema formation, and cytokine profiles.

Results

Porcine and human lung function was stable during 36-hours of NPV-ESLP with mean PF ratios throughout preservation of 473 ± 11.79 and 554.7 ± 13.26, respectively (mean ± SEM). In porcine lungs, the average compliance (Cdyn) during ESLP was 33.96 ± 2.18, mean pulmonary artery pressure (PAP) 13.03 ± 0.53, and pulmonary vascular resistance (PVR) 481.20 ± 21.86. In human lungs, the average Cdyn was 82.68 ± 3.54, mean PAP 6.00 ± 0.33, and mean PVR 184.00 ±9.71. Average percentage weight-gain/hour after 36-hours of ESLP was 1.64 ± 0.73 in the porcine group and 3.24 ± 0.19 in the rejected human lungs.

Conclusion

NPV-ESLP can preserve porcine lungs and rejected human lungs for 36-hours with acceptable physiologic function. The significant difference in weight-gain between porcine and human lungs is likely due to the rejected status of the human lungs with prolonged ischemic time prior to ESLP.

Abstracts - Oral Presentation

Small molecule AT7867 promotes pancreatic progenitor differentiation of human pluripotent stem cells for the treatment of diabetes

Nerea Cuesta-Gomez[1,2], Kevin Verhoeff[1,2], Nidheesh Dadheech[1,2], Braulio Marfil-Garza[1,2], Ila Tewari Jasra[1,2], Rena Pawlick[1,2], Haide Razavy[1,2] , AM James Shapiro[1,2]

1. Alberta Transplant Institute
2. Alberta Diabetes Institute

Introduction

Pluripotent stem cells offer the potential to provide an unlimited source of islets for the treatment of diabetes. Generation of high-quality pancreatic progenitor cells (PPs) is critical to the success of this approach. Despite recent advancements, current differentiation protocols fail to generate sufficiently pure PPs. Herein, we show that the AKT inhibitor AT7867 enhances PP cell differentiation.

Methods

We performed PP differentiation in the presence or absence of AT7867. Control and AT7867-treated PPs were characterized and compared at protein (flow cytometry, immunohistochemistry, and western blot) and transcriptional (RT-PCR) level. Control and AT7867-treated PPs were transplanted in diabetic mice, and mice were monitored for diabetes reversal defined by reversal of hyperglycemia.

Results

AT7867 treatment significantly increased the expression of PP markers (Pdx1+Nkx6.1+ and Pdx1+GP2+) in PP cells treated with AT7867 (control: 50.34% ± 7.18%, AT7867: 86.08% ± 7.73%, p=0.0087; and control: 15.82 ± 3.44, AT7867: 84.81 ± 1.54, p<0.0001, respectively). AT7867 treatment upregulated Pdx1 (p=0.0001), Nkx6.1 (p=0.0005) and GP2 (p=0.002) transcript levels compared to controls, while off-target markers PODXL (p<0.0001) and TBX2 (p<0.0001) were markedly downregulated. Notably, transplantation of AT7867-treated PPs resulted in faster reversal of hyperglycemia (within 7 weeks) in diabetic mice compared to the control group (11 weeks) (p<0.0001).

Conclusion

AT7867 improved differentiation efficiency of iPSCs into PPs at protein and transcript level resulting in faster diabetes reversal upon transplantation. In conclusion, AT7867 has the potential to generate pure PP cells for successful clinical implementation.

Abstracts - Oral Presentation

Exploring local immune modulation with rapamycin-eluting microparticles to preserve islet graft function in mice

Jordan Wong [1,2,3], Purushothaman Kuppan[1,2], Jessica Worton[1,2], Chelsea Castro [1,2], Karen Seeberger[1,2], Kateryna Polishevska[1,2], Joy Paramor [1,2], Gregory S Korbutt[1,2*], Andrew R Pepper [1,2,3*]

1. Alberta Diabetes Institute, University of Alberta, Edmonton, Alberta, Canada
2. Department of Surgery, University of Alberta, Edmonton, Alberta, Canada
3. Alberta Transplant Institute, Edmonton, Alberta, Canada
*Senior authors

Background
Islet transplantation is an effective means for a subset of people living with type 1 diabetes to achieve insulin independence; however, lifelong systemic immunosuppression required to subvert the immune response remains a major barrier to patient inclusion. Herein, we explore the use of a localized drug delivery system to preserve islet allograft function, reducing the need for toxic systemic immunosuppression.

Methods
Rapamycin (rapa), a systemic immunosuppressant used in clinical islet transplantation, was encapsulated in Food and Drug Administration-approved poly(lactide-co-glycolide) (PLGA) microparticles. We assessed the in vitro and in vivo effects of our rapa-eluting microparticles on islets with the Seahorse XF24 assay and murine islet transplants models, respectively.

Results
Human islets co-cultured 24hr with rapa-microparticles (1.0 and 2.0mg) demonstrated comparable mitochondrial potency and glucose-stimulated respiration to untreated islets, while 25 nM rapa incubation blunted the glucose response and increased proton leak. Syngeneic islets co-transplanted with 0.1 mg/kg dose rapa-microparticles (n=3) under the kidney capsule of diabetic BALB/c mice all achieved euglycemia and a 0.2 mg/kg rapa-microparticle dose (n=8) demonstrated partial function. Islet allograft recipients receiving 0.1 mg/kg rapa-microparticles (n=6) demonstrated prolonged allograft survival compared to empty microparticle recipients (n=4) (p<0.01). Rapa-microparticles + CTLA-4-Ig (n=6) resulted in 100% allograft survival at 100 days compared to 38% empty microparticles + CTLA-4-Ig (n=8)(p<0.01).

Conclusion
Our novel rapa-eluting microparticles prolonged allograft function and worked synergistically with CTLA-4-Ig therapy. Collectively, localized drug delivery has the potential to alter the immune environment, protect grafts, and may serve as a safe adjuvant approach in clinical islet transplantation.

Abstracts - Oral Presentation

The role of sex and T cells in natural vs induced ABO antibody production in mice

Ibrahim Adam[1,2,3], Bruce Motyka [1,3], Kesheng Tao[1,3] Lori West[1,2,3]

1. Alberta Transplant Institute 2. Canadian Donation and Transplantation Research Program 3. University of Alberta

Introduction

Interaction of 'natural' ABO antibodies (nAbs) with their cognate AB(H)-antigens (Ags) poses a high risk of rapid rejection of ABO-incompatible (ABOi) organ transplants. We previously demonstrated that a clear understanding of factors influencing ABO nAbs is crucial for successful ABOi heart transplantation. Here we investigated anti-A nAbs vs. intentionally-induced Abs (iAbs) with regard to role of sex and T cell requirement.

Methods

Adult wild-type (WT) and CD4 T cell knock-out (CD4KO) mice (C57BL/6 (B6) background) received weekly i.p. injection x3 of human ABO-A blood cell membranes (Hu-A BCM; 100ul of 10% v/v) or left untreated. Serum anti-A Ab was measured by hemagglutination assay using ABO-A erythrocytes from our A-transgenic mouse line. To test for T cell help and/or suppression, sex-matched CD4+ T cells (8-12×106/mouse) or CD4+CD25+ T cells (1.7-2.8×106/mouse) from spleens of WT mice were transferred to CD4KO mice. After adoptive transfer, CD4+ T cell reconstitution in peripheral blood was confirmed and mice were left untreated or challenged with Hu-A BCM and assessed for anti-A Ab.

Results

In contrast to WT mice, untreated CD4KO females produced dramatically more anti-A than males, rising substantially with puberty, and this was significantly suppressed in both sexes by adoptive transfer of sex-matched CD4+ T cells. Unlike WT mice, attempted sensitization of CD4KO mice with Hu-A BCM failed to induce additional anti-A beyond the already high levels in either sex; CD4+ T cell adoptive transfer rendered CD4KO mice responsive to A-sensitization. CD4+CD25+ T cell transfer into CD4KO mice neither suppressed anti-A nAbs nor rendered them responsive to A-sensitization (Figure).

Conclusions

When ABO 'natural' antibodies are discriminated from intentionally induced Abs, several important findings emerge: 1) Anti-A nAbs are produced without CD4+ T cell help in a sex- and age-dependent manner, suggestive of a role for sex hormones in regulating anti-A nAbs. 2) CD4+ T cells, but not CD4+CD25+ regulatory T cells, down-regulate anti-A nAb production. 3) In contrast to anti-A nAbs, production of anti-A iAbs was CD4+ T cell-dependent without a sex bias.

Abstracts - Oral Presentation

Right ventricular dysfunction by echocardiography is an early marker of evolving Cardiac Allograft Vasculopathy in heart transplanted children

Judith Namuyonga[1,2], Aslak Widerøe Kristoffersen[3,4], Nassiba Alami-Laroussi[3] , David Youssef[3] , Jennifer Conway[3] , Michael Khoury[3] , Lily Lin[3], Luke Eckersley [3], Nee Scze Khoo , [3] Simon Urschel[3]

1. Uganda Heart Institute, Kampala, Uganda
2. College of Health services, Makerere University, Kampala, Uganda.
3. University of Alberta and Stollery Children's hospital, Edmonton, AB
4. Department of Pediatric Cardiology, Division of Pediatric and Adolescent Medicine, Oslo University Hospital, Oslo, Norway

Purpose

Cardiac allograft vasculopathy (CAV), is the leading cause of late graft loss after pediatric heart transplant (HTx). Coronary angiography, the gold standard for diagnosis is invasive, requires anesthesia and can cause adverse events. Non-invasive methods can identify acute rejection, but their utility in detecting CAV is not known. We investigated functional echocardiography (FE) as a tool to identify CAV.

Methods

Using a prospective database collecting standardized FE in HTx children (<18y) between 2005 and 2020 we compared 10 patients diagnosed with CAV by ISHLT criteria with 10 controls matched for age, time post-HTx, pre-HTx disorder, without CAV (CON). We compared FE in absence of acute rejection at the time of CAV diagnosis and 6-12 months prior (PRE) using non-parametric and FIsher's exact test.

Results

CAV and CON were similar for age (median 8.5y vs 8y), sex, pre-HTx doiagnosis, time since HTx and immune suppressive regimen. Two controls had undergone HLA desensitization therapy pre HTx, none in the CAV group. CAV patients were more likely to have a history of acute rejection (5 Acute cellular, 2 Antibody mediated vs 2/0)and have Class II HLA donor specific antibodies. At CAV diagnosis as well as PRE, right ventricular longitudinal strain and strain rate were reduced compared to controls (p<0.05). RV fraction of area change was reduced at CAV diagnosis (p<0.01) but not PRE comapred to controls. No diference between groups was found for LV Ejection Fraction and LV-strain measurements, however LV medial E/e' was increased at CAV (p<0.02) but no PRE.

Conclusion

Using FE, LV-diastolic and multiple RV markeres are abnormal in children at presentation of CAV compared to controls with stable graft function. Interestingly, echocardiographic deformation imaging revealed RV abnormalitites 6 to 12 months prior to CAV diagnosis, suggesting RV-FE may support earlier and non-invasive detection of CAV.

Abstracts - Oral Presentation

Statin Use in Liver Transplant: Indication, Use and Impact of Statins on Patient Outcomes

Matthew K. Smith[1], Cora Laidlaw[2], Juan G. Abraldes[3], Rahima A. Bhanji[3]

1. Division of Gastroenterology, University of Alberta, Edmonton, AB
2. Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB
3. Liver Unit, Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada

Background

Cardiovascular and metabolic disease are prevalent among patients with chronic liver disease and contribute to mortality and adverse outcomes. In our study, we aimed to evaluate the indication and rate of statin use in patients both pre and post liver transplant as well as the impact on post-transplant survival, graft failure, cardiovascular and metabolic adverse events.

Methods

We identified a retrospective cohort of 868 adult liver transplant recipients in one tertiary transplant centre in Edmonton, Alberta, Canada between 2005 and 2020. Primary endpoints included rate of statin use, post-transplant patient survival, and graft failure; secondary endpoints included development of cardiac disease, dyslipidemia, metabolic syndrome post-transplant.

Results

In the pre-transplant period only 3% of patients were on statin therapy despite 33% having an indication. Post-transplant, 29.9% were placed on statin therapy despite 53% having indication. The use of statin post-transplant was associated with decreased mortality (OR 0.433, 95% CI [0.302-0.622]) and decreased graft failure (OR 0.398, 95% CI [0.276-0.574]), it was also associated with increased graft rejection (OR 1.40, 95% CI [1.02-1.93]). There were no significant differences in secondary endpoints.

Conclusion

In our retrospective cohort study we identified an association between statin use in the post-transplant setting and improved mortality and graft survival, though it was not associated with improved rates of rejection or cardiac and metabolic outcomes. We also identified a discrepancy between the number of patients with indication for statin use from those who were on statins both pre and post liver transplant, reflecting under utilization.

Abstracts - Oral Presentation

Molecular features of baseline lung allograft dysfunction

Martina Mackova[1], Patrick Gauthier[1], Jessica Chang [1], Greg Snell [2], Glen Westall [2], Stephen Juvet[3], Jan Havlin [4], Phil Halloran [1], Kieran Halloran[1]

1. University of Alberta, Edmonton, Canada
2. Alfred Hospital, Melbourne, Australia
3. University Health Network, Toronto, Canada
4. University Hospital Motol, Praha 8, Czech Republic

Background

Baseline lung allograft dysfunction (BLAD) is a physiologic state post-lung transplant where lung function fails to reach normal thresholds and is associated with a dose-dependent increase in risk of death. The mechanisms of BLAD are not understood. We sought to characterize the gene expression associated with BLAD in transbronchial biopsies taken from a large prospective cohort of lung transplant recipients.

Methods

We studied 536 transbronchial biopsies (TBBs) four international centers. We defined BLAD as per our previously published definition. We analyzed the top transcripts and pathogenesis-based transcripts (PBT) associated with BLAD status. We used 10-fold cross cross-validation to generate an optimized model based on top transcripts to predict BLAD status at 1-year post-transplant.

Results

BLAD was present in 221 (41%) biopsies from 184 patients, consistent with prior estimates. Patients with BLAD were more likely to have a history of interstitial lung disease and severe primary graft dysfunction, and to progress to graft failure. The top transcripts increased or decreased in BLAD were mainly associated with parenchymal function. PBTs in biopsies obtained within the first post-transplant year had increased injury repair, macrophage, and rejection-associated transcripts. Biopsies > 1-year post-transplant showed no PBT associations. A molecular BLAD classifier based on top transcripts predicted BLAD status with an AUC of 0.61.

Conclusions

BLAD status was associated with increased macrophage and rejection transcripts in biopsies taken within 1-year post-transplant. We hypothesize this is because some BLAD is intrinsic to the lung tissue, while some is extrinsic (diaphragms, chest wall, large airways).

Abstracts - Oral Presentation

DSA-Negative Microvascular Inflammation in Kidney Transplant Biopsies: Gene Expression Comparison with Native and Transplant Kidney Controls

Anna Buxeda[1,2], Ivy Fixsen[1] , Ian Gibson[3] , Chris Wiebe[4] , Peter Nickerson[4] , Patricia Campbell[1] , Julio Pascual[5] , Marta Crespo[2] , Michael Mengel[1] , Benjamin Adam[1]

1. Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB
2. Department of Nephrology, Hospital del Mar, Barcelona, Spain
3. Department of Pathology, University of Manitoba, Winnipeg, MB
4. Department of Internal Medicine, University of Manitoba, Winnipeg, MB
5. Department of Nephrology, Hospital Universitario 12 de Octubre, Madrid, Spain

Background

Kidney transplant biopsies occasionally demonstrate histological features of microvascular inflammation (MVI), suggestive of antibody-mediated rejection (ABMR), but without identifiable anti-HLA donor-specific antibodies (DSA). This suggests that the MVI may be caused by non-alloimmune etiologies such as ischemic injury. The aim of this study was to further understand the significance of these changes through biopsy-based molecular characterization.

Methods

NanoString nCounter was used to compare the expression of six gene sets in 150 archival FFPE kidney transplant biopsies, including with MVI (g+ptc>1) but no identifiable DSA (MVI, n=42), antibody-mediated rejection with DSA (ABMR, n=22), pure T-cell mediated rejection without DSA (TCMR, n=10), mixed MVI and TCMR without DSA (MVI+TCMR, n=43), normal implant biopsies (Normal, n=11), and native kidney biopsies with either endocapillary proliferative glomerulonephritis (GN, n=12) or minimal change disease (MCD, n=10). The gene sets included transcripts previously associated with ABMR, DSA (DSAST), endothelial injury (ENDAT), TCMR, early injury, and late injury.

Results

Principal component analysis demonstrated significant molecular overlap between sample groups. DSA-negative MVI, MVI+TCMR, and TCMR demonstrated similar ABMR gene set expression compared with ABMR (p>0.05), but higher expression than GN ($p \leq 0.008$) and Normal ($p \leq 0.004$). DSAST and ENDAT gene set expression was also similar between ABMR, MVI, and MVI+TCMR. TCMR and early injury gene set expression was higher in TCMR than all other groups ($p \leq 0.002$), except MVI+TCMR.

Conclusions

These results suggest that, similar to their histological overlap, kidney transplant biopsies displaying MVI with and without detectable DSA have similar molecular phenotypes, including with transcripts historically associated with ABMR.

Abstracts - Virtual Poster

IMPACT OF DIABETES ON POST LIVER TRANSPLANT OUTCOMES

Muhammad Imran Suliman [1], Dr. Rahima Bhanij [2], Prof. Juan G. Abraldes [2,3,4]

1. Core Internal Medicine, University of Alberta.
2. Division of Gastroenterology, Liver Unit, University of Alberta
3. Cirrhosis Care Clinic, Division of Gastroenterology (Liver Unit), Cegiir, University of Alberta
4. Cirrhosis Care Clinic, Division of Gastroenterology (Liver Unit), University of Alberta, Centre of Excellence for Gastrointestinal Inflammation and Immunity Research, Edmonton, AB

Background

Metabolic Syndrome in Liver transplant (LT) candidates has an impact on long-term outcomes including post-LT morbidities {cardiovascular (CVD) and renovascular complications} and poor graft and patient survival.1 Likewise, de novo appearance of Diabetes Mellitus (DM) , may lead to poor outcomes after LT.2,3 There is a paucity of studies assessing the impact of DM post-LT, subsequent management of the blood sugar control, and incidence of micro and macrovascular complications on graft or patient survival. Aims To investigate the impact of pre-LTDM and its management on long-term outcomes following LT.

Methods

Adult patients who underwent their first LT between 2016 to 2020, at the University of Alberta, were analyzed. Data for pre-LT DM (diabetes and type, glycated hemoglobin levels (HBA1c), and pharmacotherapy), cardiovascular disease, and chronic renal disease were reviewed.

Results

A total of 338 patients were analyzed; 66% were females with a mean age of 53 years (SD 12) at LT. Those with pre-LT DM (23%) and without it (77%) were similar in terms of sex and race. Patients with pre-LT DM were more likely to have NASH cirrhosis (35% vs. 10%; p < 0.001) and HCC (52% vs. 24%; p < 0.001). They were less likely to have autoimmune liver disease (AILD) (13% vs. 26%; p= 0.014), present with acute liver failure (ALF) (5% vs 15%; p= 0.02) or hepatorenal syndrome (HRS) (8% vs. 17%; p=0.046). Pre-LT median HBA1c was available for 77% of the patients and was 5.8 [5.1, 7.1]. More than half (54%) were on insulin and 60% were on metformin. Pre-LT DM patients were more often diagnosed with hypertension, dyslipidemia, metabolic syndrome (MS) and pre-LT cardiovascular disease. Following LT, HBA1c was available for 72% at 1 year (median 7.0 [6.1, 7.7]). De novo DM occurred in 10 (3.9%) of the patients. There was a trend to increased CVD in patients with DM (15% vs. 8%; p = 0.08), but there was no difference in time to CV event (683 days [252, 1524] vs. 565 days [43, 948]; p=0.67). Patients with pre-LT DM were more likely to have CKD at 6 and 36 months (Table #1). In multivariable analysis, pre-LT DM was associated with CKD at 6-months (OR 1.8 [1.0, 3.1]; p = 0.04) and at 36- months (OR 2.3 [1.01, 5.05]; p = 0.048). Having pre-LT DM did not have a significant impact on rejection, graft or patient survival. However, patients with pre-LT DM were more likely to die from renal complications (2.5% vs 0 %; p = 0.05).

Conclusions

Pre-LT DM was present in 23% of the patients; 72% of patients had HBA1c at 1 year post-LT with levels within acceptable target. De novo DM only occurred in 3.9% of patients, which is much lower than reported rates 4 This may be due to our centre being corticosteroid free (only 25% of patients were on steroids). Presence of pre-LT DM was associated with presence of CKD, but did not impact graft or patient survival.

Abstracts - Virtual Poster

Non-linear mixed-effects modeling to characterize the interaction between renal function and mycophenolic acid clearance in pediatric kidney transplant recipients

Yan Rong [1], Jenny Wichart [2], Lorraine Hamiwka [3], Tony Kiang [1]

1. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB
2. Alberta Health Services, Pharmacy Services, Calgary, AB
3. Department of Pediatrics, Cumming School of Medicine, University of Calgary, Calgary, AB

Background

Mycophenolic acid (MPA) is an immunosuppressant widely used in pediatric kidney transplantation. The commonly observed large variabilities in MPA plasma exposure can lead to adverse drug effects. The objective of this study was to establish a non-linear mixed-effects model to characterize the population estimates and the influence of clinical covariates on the pharmacokinetics of MPA in pediatric kidney transplant patients.

Methods

This was a retrospective pharmacokinetic study using data collected from pediatric kidney transplant patients (≤18years of age) at Alberta Children's Hospital (Calgary). Stochastic approximation expectation-maximization was conducted in Monolix2021R2 (Lixoft SAS, France) using already established workflows (e.g., Rong Y, Mayo P, Ensom MHH, Kiang TKL; Clin Pharmacokinet. 2019;58(11):1483-1495).

Results

A total of 50 pediatric kidney transplant patients (female:male= 25:25) with 219 MPA plasma concentration-time profiles were included. The average age (±standard deviation) and post-transplant time were 12.8±4.8years and 762±1160days, respectively. Of the 216 models tested, a two-compartment, first-order absorption with lag time, and linear elimination structural model of MPA best described this population. The absorption rate constant (2.52h-1), lag time (0.166h), volumes of distributions of the central (27.24L/h) and peripheral (389.13L/h) compartments, and inter-compartment clearance (19.2L/h) were consistent with literature values. Of the 16 covariates tested, only estimated glomerular filtration rate (eGFR) was a significant covariate affecting total MPA clearance (i.e., 0.72L/h, positive relationship).

Conclusion

This is the first evidence demonstrating a positive relationship between total MPA clearance and eGFR using population pharmacokinetic modeling in pediatric subjects. The underlying mechanisms are being investigated by our group.

Abstracts - Virtual Poster

Enzyme induction effects of corticosteroids on the intrinsic clearance of mycophenolic acid in a human hepatoma cell line

Yan Rong[1] , Tony Kiang[1]

1. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

Background
Mycophenolic acid (MPA) is commonly prescribed for the prevention of graft rejection post-transplantation. MPA is frequently combined with prednisone/prednisolone as the maintenance immunosuppression regimen. Despite multiple reviews having suggested potential induction effects of corticosteroids on the metabolism of MPA, definitive evidence confirming this interaction is lacking (Rong and Kiang. Clin Pharmacokinet. 2023; 62:157-207). We hypothesized that prednisone/prednisolone can induce the metabolism of MPA (i.e., increasing the formation of the MPA-glucuronide [MPAG] metabolite) in a human hepatoma cell line.

Methods
Metabolically competent HepaRG cells were maintained/differentiated as per manufacture's protocol (0.4million/well in 24-well plates). The cells were pre-incubated with rifampicin (20 and 100µM, positive control), prednisone (40, 80, and 400µg/L), or prednisolone (200, 800, and 2000µg/L) for 3 or 6 days prior to treatment with MPA (1.5-hour incubation, 0.4µg/mL [linear conditions]). Cell medium was refreshed every 24 hours. Concentrations of MPA and MPAG were determined using a validated liquid-chromatography tandem mass spectrometry assay in our lab.

Results: For all tested conditions, the duration of pre-incubation did not affect MPAG production or MPA depletion. For the positive control, 100µM rifampicin (6-day pre-incubation) increased MPAG formation by 68.3±14.5% (mean±standard deviation, p<0.05) while decreasing MPA concentrations by 43.9±5.4%. Prednisone (400µg/L) and prednisolone (2000µg/L) generated 14.5±22.4% and 54.2±9.6% increases in MPAG formation (6-day pre-incubation) and 18.7±8.9% and 30.4±10.0% reductions in MPA concentrations, respectively.

Conclusion
To our knowledge, this is the first evidence supporting the induction effects of corticosteroids on the intrinsic clearance of MPA. Further mechanistic investigations are ongoing in our laboratory.

Abstracts - In-person Posters

Risk Factors for Thromboembolic Events in Pediatric Patients with Ventricular Assist Devices

Jeremy Adderley [1], Tara Pidborochynski [2], Holger Buchholz [3], Paula Holinski [4], Vijay Anand [4], Izak De Villiers Jonker [5], Darren H. Freed [3,5], Mohammed Al-Aklabi [5], Jennifer Conway [2,6]

1. Faculty of Medicine and Dentistry - University of Alberta
2. Department of Pediatrics - University of Alberta
3. Department of Cardiac Surgery - University of Alberta
4. Division of Pediatric Critical Care, Stollery Children's Hospital
5. Division of Pediatric Cardiac Surgery, Stollery Children's Hospital
6. Division of Pediatric Cardiology, Stollery Children's Hospital

Background

Pediatric patients on ventricular assist device (VAD) support are at risk of thromboembolic (TE) complications including pump thrombosis, ischemic stroke, and transient ischemic attack.

Methods

We conducted a retrospective chart review of pediatric patients implanted with Paracorporeal Pulsatile (PP) or Paracorporeal Continuous (PC) VADs between 2005-2022, at the Stollery Children's Hospital (Edmonton, AB). Patients that transitioned from PC to PP were classified in a combination group. Patient and device-related factors, including initial anti-coagulation strategies were collected. Kaplan Meier (KM) survival analysis was performed to determine freedom from TE event based on initial anti-coagulation strategy and VAD type. Univariate and multivariate Cox proportional hazard analysis was conducted to look for factors associated with TE events.

Results

Of the 95 patients included, median age was 0.92 years (IQR 0.27, 5.37), median weight at implant was 8.4 kg (IQR 4.4, 18.0). Almost two-thirds (63%) had non congenital disease, with 47% supported on PC devices, 25% on PP devices, and 28% with a combination of devices. Initial anti-coagulation was with either Heparin (61.5%) or Bivalirudin (38.5%). Unadjusted freedom from a TE event was significantly higher in those who received Bivalirudin as their initial anti-coagulation strategy (p=0.022, Figure1). KM analysis based on device type found that PC VADs predicted shorter freedom from TE events (p=0.012). In multivariate analysis, initial anticoagulation strategy (HR 0.359, 95% CI 0.165-0.785, p=0.01) for Bivalirudin was protective against events, while device type (HR 10.9, 95% CI 2.68-44.2, p<0.001), specifically PC devices, was found to be a predictor of TE events.

Conclusions

This study suggests that device type, particularly PC, and heparin as an initial anti-coagulation strategy are risk factors TE events. Further work is needed to understand the interaction between device type and initial anti-coagulation strategy.

Abstracts - In-person Posters

Donor CD11c cell depletion increases chimerism in neonatal mice tolerized with an allogeneic spleen/bone marrow protocol involving peripheral CD8 T cell depletion and CD154 co-stimulation blockade

Roger Bascom[1,2], KeSheng Tao[1,2], Lori West[1,2]

1. Alberta Transplant Institute
2. Department of Pediatrics, University of Alberta

Background
Tolerance is induced in allogeneic spleen (SC)- and bone marrow (BMC)-injected neonatal mice by CD8 T cell depletion with CD4 T cell co-stimulation blockade. To increase donor cell chimerism and robustness of induced tolerance, we further inhibited direct activation of host CD4 T cells by depleting donor dendritic cells (DC) from the adult tolerizing inocula.

Methods
Neonatal C3H (H-2k) mice were injected with CD8a (53-6.7) and CD154 (MR1) antibodies in addition to adult CD8/NK cell depleted GFP+ B6 (H-2b) SC/BMC ± CD11c cells. Treated mice were transplanted as adults with donor-type hearts.

Results
5/5 B6 hearts transplanted into neonatally-treated (allo-SC/BMC with CD8 depletion/CD4 co-stimulation blockade) adult C3H mice beat at d100, but two did so with diminished strength (2+/1.5+ out of 4+). Additional depletion of DC from adult inocula increased donor GFP+ chimerism in skin, thymus, kidney and bone on d6, but not in other organs, as determined by whole body and organ imaging. At d6, chimerism in spleen included T and B cells located in PALS and follicular regions respectively. GFP signal in skin on d6 was "spotty" rather than uniform and by high resolution microscopy included donor T cells (CD3+) and macrophages (F4/80+). In contrast, chimerism in neonatal thymus on d6 included donor DC and T cells, suggesting tolerance induction. Consistent with tolerance induction, all B6 donor-type hearts transplanted into treated C3H mice (n=3) continued to beat at d100 with high scores (4+/3.5+/3+).

Conclusion
Added donor DC depletion in the allo-SC/BMC tolerizing procedure enhances neonatal tolerance induction.

Abstracts - In-person Posters

Changes In Renal Function After Islet Transplantation In A Single-Centre Cohort In Canada Over 20 Years

Alice L. J. Carr[1,2], Braulio A. Marfil-Garza[1], Ying Ling[1] , Richard A. Oram[2] , Tolulope O. Olateju[1], Anna Lam[1,3], Khaled Dajani[3] , Blaire Anderson[3], Doug O'Gorman[3], Tatsuya Kin[3], David Bigam[3], A.M. James Shapiro[3], Peter A. Senior[1,3]

1. Alberta Diabetes Institute, University of Alberta, Edmonton, Canada
2. Institute of Biomedical and Clinical Science, University of Exeter Medical School, Exeter, UK
3. Clinical Islet Transplant Program, University of Alberta, Edmonton, Canada

Background

Long term data on renal function after islet transplantation (ITx) remains scarce.[1] Herein, we assessed renal function over a period of up to 20 years after ITx.

Methods

We included 225 ITx recipients at the University of Alberta Hospital. We calculated individual mean estimated glomerular filtration rate (eGFR) for 12mo prior to transplant (baseline) and monthly post-first transplant. We assessed decline in eGFR using mixed effects models with random effects during ≤1y, 1-5y and 5-20y post-first transplant. In addition, we assessed eGFR decline stratified by pre-transplant eGFR: high (≥60 ml/min/1.73m2) and low (<60 ml/min/1.73m2). We assessed progression to Stage 4 CKD (S4CKD, eGFR <30 ml/min/1.73m2) using multivariable Cox proportional hazard regression.

Results

In our cohort, 41% were male, with a median (IQR) age-at-transplant of 49y (42,55), a duration of T1D of 30y (22,39), and baseline eGFR of 87 ml/min/1.73m2 (72,97). The steepest monthly eGFR decline occurred ≤1y post-transplant (≤1y: -0.92 [95%CI, -1.02,-0.82]; 1-5y: -0.25 [95%CI, -0.27,-0.24]; 5-20y: -0.11 [95%CI, -0.11,-0.1]). Recipients with high baseline eGFR experienced steeper monthly decline compared to those with low eGFR during ≤1year post-first transplant (-0.99 [95%CI, -1.09,-0.88] vs -0.36 [95%CI, -0.67,-0.04], p<0.001) with no differences thereafter. Progression to S4CKD occurred in 7.3%, with higher hazard for those with low eGFR at baseline (HR 10.5 [95%CI, 2.89,38.0], p<0.001). Progression to end-stage renal disease was rare (2.8%).

Conclusion

Decline in renal function is greatest ≤1y post-first ITx. Recipients with reduced baseline renal function do not experience steeper eGFR declines post-transplant, however, are at higher risk of progression to S4CKD.

Abstracts - In-person Posters

OPAL - Online Prehabilitation for Patients Awaiting Liver transplantation - A multicentre randomized controlled trial to reduce physical frailty and improve health outcomes

Christofer Cruz [1], Puneeta Tandon [1], Margaret L. McNeely[2]

1. Division of Gastroenterology (Liver Unit), Department of Medicine, University of Alberta, Edmonton, AB
2. Department of Physical Therapy, University of Alberta, Edmonton, AB

Background

Physical frailty is common in patients awaiting liver transplantation (LT) and has been associated with poor health outcomes. Small studies show that prehabilitation can improve physical function in patients while waiting for LT. In this multicentre RCT, we will assess the impact of a 12-week behaviour change informed online nutrition and exercise prehabilitation program (OPAL) in n=~216 adults awaiting LT on the primary outcome of the six-minute walk test and additional outcome measures.

Methods

Inclusion criteria: 18+, have cirrhosis, pre-frail or frail on the liver frailty index, listed or likely to be listed for LT, and own an internet connected device. Participants will be randomly assigned to the intervention or to usual care (2:1 allocation). Usual care participants will receive an online resource package. Intervention participants will receive a prehabilitation program delivered via an online web platform called Heal-Me, consisting of nutrition and exercise group classes and in-platform activities. Secondary/exploratory outcomes include frailty, malnutrition, sarcopenia, covert hepatic encephalopathy, health-related quality of life, post-transplant outcomes, a basic economic evaluation and end-of-study qualitative interviews.

Results

Ethics is approved at the University of Alberta site and Ethics applications are underway across five other transplant programs across Canada. The estimated study start date is end of May 2023.

Conclusions

While prehabilitation is standard of care for some pre-transplant organ groups, we currently lack large scale RCTs in prehabilitation in LT candidates. The OPAL trial will bring Canadian LT centres together to advance our knowledge around the impact and acceptability of prehabilitation pre-LT.

Abstracts - In-person Posters

Parental Perceptions of Ex-Situ Heart Perfusion

Sadie Deschenes [1], Michael van Manen[2,3], Tara Pidborochynski [2], Darren H. Freed[4], Jennifer Conway[2,5]

1. Faculty of Nursing, University of Alberta
2. Department of Pediatrics, University of Alberta
3. John Dossetor Health Ethic Centre, University of Alberta
4. Department of Cardiac Surgery, University of Alberta
5. Division of Pediatric Cardiology, Stollery Children's Hospital

Introduction

Pediatric heart transplant (HTx) candidates continue to have high waitlist mortality due to donor availability. Ex-situ heart perfusion (ESHP) has the potential to increase the donor pool, yet has been used sparingly in pediatrics due to size restrictions of the current technology. Previous work has shown that for ESHP to be accepted by pediatric healthcare providers (HCP), the risks to the donor heart and the costs need to be better understood and that rigorous research and implementation oversight is essential. Perspectives from caregivers about ESHP has not been assessed and forms the basis of this qualitative study.

Methods

Virtual, semi-structured interviews were conducted with caregivers of children who are awaiting or received HTx. Data were analyzed using qualitative content analysis.

Results

Twelve participants from 2 countries participated in this study. Awareness about and understanding of ESHP varied among participants from complete unawareness to understanding specifics. Independent of their awareness, all purported that it was an excellent and innovative technology, and supported ESHP implementation in pediatrics. No ethical issues or concerns about the use were identified that differed from other medical technologies, although participants did state that understanding the length of time the heart can be mounted and risks to donor and recipient were important. Participants expressed various views on how to approach parents regarding ESHP. Overall, most participants stated that the consent processes should be like other medical procedure and some commented that deferred or waived consent would be acceptable, especially if ESHP became part of routine clinical practice. Even if consent was waived, participants agreed that the use of ESHP should be disclosed just like other information is disclosed about the donor heart and that introduction of ESHP should come early in the HTx journey.

Conclusion

Families are supportive of the use of ESHP. Like HCPs, they endorse the need to understand the potential risks and that information should be presented early in the transplant process.

Abstracts - In-person Posters

Enzymatic conversion of blood group A- to H-antigen in a mouse model to facilitate ABO-incompatible transplantation

Tate Erickson[1,2,3,4], Bruce Motyka[1,2,3,4], Lai Xu[1,2,3,4], Kesheng Tao[1,2,3,4], Jean Pearcy[1,2,3,4], Marcelo Cypel[4,5], Jayachandran N. Kizhakkedathu[3,4,6], Peter Rahfeld[3,7], Peter. J. Cowan[3,8], Stephen G. Withers[3,9], Lori J. West[1,2,3,4,10]

1. Department of Pediatrics, University of Alberta
2. Alberta Transplant Institute
3. Canadian Glycomics Network
4. Canadian Donation and Transplantation Research Program
5. Department of Surgery, University of Toronto
6. Department of Pathology and Laboratory Medicine, University of British Columbia
7. Avivo Biomedical Inc., Vancouver
8. Immunology Research Centre, St Vincent's Hospital Melbourne, Melbourne, Australia
9. Department of Chemistry, University of British Columbia
10. Departments of Surgery, Medical Microbiology and Immunology, and Laboratory Medicine and Pathology, University of Alberta

Background: The ABO histo-blood group limits organ availability in transplantation (Tx). Reduction of donor A/B-antigens may represent a novel approach to allow safe ABO-incompatible (ABOi) Tx. We recently demonstrated the utility of the enzymes FpDeAc and FpGalNase, termed Azymes, to convert blood group A to blood group O in an ex vivo human lung perfusion model; however, the duration of A-antigen removal remains unclear. Here we used a mouse model to assess A-antigen removal/re-expression following Azymes administration.

Methods: A-transgenic (A-Tg) mice (male/female, n=7/7; 10-44 weeks), expressing A-antigen on vascular endothelium and red blood cells (RBC), were used to study Azymes function. In vitro: RBC from A-Tg mice were assessed for A- and H-antigen expression by hemagglutination post-Azymes treatment (2-50 µg/mL, 0.5-4 hours). In vivo: A-Tg mice were injected with Azymes (0.4-0.8 mg/kg) and A- and H-antigen expression was assessed at various times (0.25-96 hours) on RBC (by flow cytometry and hemagglutination) and heart/lung (by immunohistochemistry).

Results: In vitro: Azymes fully converted A- to H-antigen on A-Tg mouse RBC. In vivo: Azymes treatment fully converted A- to H-antigen on A-Tg mouse RBC, persisting 2 hours post-treatment. Heart and lung vascular endothelium showed a marked reduction in A-antigen and conversion to H-antigen up to 8 hours post-treatment.

Conclusion: In a mouse model, A-antigen was effectively removed from RBC and heart/lung with lack of re-expression persisting several hours. Clinical application of Azymes has the potential to expand ABOi Tx, allowing lifesaving Tx in individuals for whom compatible organs may otherwise not be found.

Abstracts - In-person Posters

24-hour Negative Pressure Ventilation Ex-situ Lung Perfusion With Transplantation

Keir Forgie[1,2], Abeline Watkins [2], Katie Du [2], Alynne Ribano [2], Darren Freed [3], Jayan Nagendran[1] *(Poster Presenters: Alynne Ribano and Katie Du)*

1. Cardiac Surgery, University of Alberta, Mazankowski Alberta Heart Institute, Edmonton, AB
2.University of Alberta, Edmonton, AB
3.Stollery Children's Hospital, Edmonton, AB

Background
Clinical Ex-Situ Lung Perfusion (ESLP) is limited to 4-6 hours, and pre-clinical continuous ESLP is typically performed for 12-hours. Continuous ESLP of 24- to 48- hours is required to optimize the rehabilitation potential of ESLP as a vehicle for gene- and cell-based therapies. We describe the results of our reliable 24-hour Negative Pressure Ventilation (NPV)-ESLP protocol with transplantation in a large animal model.

Methods
Twelve sets of pig lungs underwent 24-hours of NPV-ESLP. At evaluation, a mixed gas was applied to deoxygenate the perfusate and assess lung oxygenation. Six left lungs were transplanted for in-vivo assessment over a 4-hour period. Graft function was evaluated via physiologic parameters, edema formation, and pro-inflammatory cytokine profiles.

Results
Donor lungs demonstrated stable and acceptable oxygenation after 24-hours of normothermic NPV- ESLP (PF ratio 508.0 ± 26.91; mean ± SEM). Lungs demonstrated a gradual loss in compliance over time. Average compliance was 19.53 ±2.22 after 24-hours. Mean pulmonary artery pressure (PAP) and pulmonary vascular resistance initially increased during ESLP and gradually decreased thereafter with values of 12.18 ± 1.64 and 466.7 ± 63.63 at 24-hours, respectively. Mean percentage weight-gain/hour was 3.84 ± 2.43. Following transplantation and reperfusion, isolated left lung oxygenation was excellent (320.3 ± 9.99). Isolated left lung percentage weight gain/hour was 4.77 ± 1.35.

Conclusion
Our porcine NPV-ESLP model maintained acceptable oxygenation, compliance, and vascular resistance during 24-hours of preservation. Isolated left lung assessment in the acute post-operative period resulted in satisfactory PF ratios (>300 mmHg, PGD 0-1).

Abstracts - In-person Posters

Perfusate Exchange Does Not Improve Outcomes of Negative Pressure Ventilation Ex-situ Lung Perfusion

Keir Forgie[1,2], Abeline Watkins[2], Katie Du[2], Alynne Ribano[2], Darren Freed[3], Jayan Nagendran[1] *(Poster Presenter: Katie Du)*

1. Cardiac Surgery, University of Alberta, Mazankowski Alberta Heart Institute, Edmonton, AB
2. University of Alberta, Edmonton, AB
3. Stollery Children's Hospital, Edmonton, AB

Purpose

ESLP protocols include perfusate replacement to counteract fluid loss and accumulated deleterious by-products. Perfusate replacement has not been studied in a model of Negative Pressure Ventilation (NPV)-ESLP, nor using a cellular perfusate with autologous packed red blood cells (pRBC). Perfusate exchange during NPV-ESLP may improve post-transplant lung function.

Methods

Twelve sets of pig lungs divided into two groups (n=6/group) underwent 24-hours of NPV-ESLP using 1.5 L of cellular perfusate (500mL autologous pRBC and 1L of buffered perfusate). Group 1 (Control) had no perfusate exchange. Group 2 (Perfusate Exchange, PE) had 500mL removed from the reservoir after 12-hours of NPV-ESLP and replaced with 1000mL of fresh perfusate. Three left lungs from each group were transplanted for in-vivo assessment over 4-hours.

Results

Results are Control vs PE (mean ± SEM). Both groups demonstrated acceptable oxygenation during 24-hours of ESLP with final PF ratios of 527.5 ± 42.19 and 488.4 ± 35.38 (p=0.25). There was a gradual loss in compliance over time in all lungs. Final compliance measurements were 20.52 ± 3.59 and 18.55 ± 2.91 (p=0.34). There were no significant differences in PAP after 24-hours of ESLP (10.02 ± 2.69 vs. 14.34 ± 1.64, p=0.10); however, PVR differed significantly (357.3 ± 88.37 vs. 576.0 ± 72.28, p=0.04). Percentage weight-gain/hour between groups was similar (1.01 ± 0.35 vs 1.89 ± 0.32, p=0.07). Post-transplant left lung oxygenation was excellent (327.3 ± 14.62 and 313.3 ± 15.38, p=0.28).

Conclusion

Perfusate exchange did significantly alter outcomes between groups over 24-hours of NPV-ESLP or post-transplantation.

Abstracts - In-person Posters

Mild Permissive Alkalosis Improves Outcomes In Porcine Negative Pressure Ventilation Ex-situ Lung Perfusion

Keir Forgie[1,2], Abeline Watkins [2], Katie Du[2], Alynne Ribano [2], Darren Freed[3], Jayan Nagendran[1] *(Poster Presenter: Alynne Ribano)*

1. Cardiac Surgery, University of Alberta, Mazankowski Alberta Heart Institute, Edmonton, AB
2. University of Alberta, Edmonton, AB
3. Stollery Children's Hospital, Edmonton, AB

Purpose

Clinically, mild permissive alkalosis counteracts elevated pulmonary vascular resistance (PVR) through vasodilation. We have observed an initial increase in PVR and pulmonary artery pressure (PAP) during porcine ESLP that mirrors a rise in pro-inflammatory cytokines. Increased hydrostatic pressure can worsen edema and lung compliance. We hypothesized that mild permissive alkalosis may improve outcomes in ESLP.

Methods

Twelve pig lungs (50kg) underwent 12-hours of Negative Pressure Ventilation (NPV)- ESLP targeting a physiologic pH (Control: pH 7.35-7.45, n=6) or mild permissive alkalosis (pH+: pH 7.45-7.55, n=6) through varying the delivery of CO2. At evaluation, lung oxygenation was assessed with a mixed sweep gas to deoxygenate the perfusate. Three left lungs from each group were transplanted and assessed over 4-hours.

Results

Results are pH+ vs Control. Both groups had acceptable oxygenation (PaO2/FiO2 454.2 vs 438.2; p=0.37) and dynamic compliance (21.38 vs 22.22 ml/cmH2O; p=0.41) over 12-hour NPV-ESLP. Mean evaluation pH/pCO2/HCO3- were 7.50/15.6/14.5 vs 7.41/38.7/24.7. Mean PAP was similar (10.89 vs 14.12; p=0.19) as was PVR (438.60 vs 557.9; p=0.21). Control lungs required THAM, nitroglycerin, and milrinone to manage elevated PVR. Weight-gain/hour was similar (1.23% vs 1.38%; p=0.37). Mean left lung PF ratios 4-hours post-transplantation were 301 mmHg vs 196 mmHg (p=0.11). Control TNF-α perfusate concentrations were significantly greater at 1 (p=0.02) and 3 (p=0.04) hours of ESLP. Five Control lungs failed on ESLP (T5-T8) due to high PAP.

Conclusion

Mild permissive alkalosis porcine NPV-ESLP demonstrated more reliable ESLP preservation with reduced inflammation. Mild alkalosis may protect highly reactive pig vasculature through vasodilation.

Abstracts - In-person Posters

Beyond the hemagglutination assay for ABO-histocompatibility: ABH-glycan-functionalized beads allow precise characterization of ABO antibodies

Anne M. Halpin[1,2,3,4,5,6], Bruce Motyka[1,4,5,6], Jean Pearcey[1,4,5,6], Caishun Li[1,4,5,6], Tess Ellis[1,4,5,6], Todd Lowary[4,6,7], Chris Cairo[4,6,7], Lori J. West[1,2,4,5,6]

1. Department of Pediatrics, University of Alberta
2. Department of Laboratory Medicine and Pathology, University of Alberta
3. Alberta Precision Laboratories
4. Canadian Glycomics Network
5. Alberta Transplant Institute
6. Canadian Donation and Transplantation Research Program
7. Department of Chemistry, University of Alberta

Background

Immune risk assessment in transplantation has been revolutionized by HLA single antigen Luminex beads. ABO-incompatible (ABOi) transplantation relies on ABO antibody (ABO-Ab) quantification by hemagglutination assay (HA), plagued by poor reproducibility and limited ability to distinguish IgG vs IgM isotypes; A/B-glycan-subtype specificities of ABO-Abs cannot be determined. Aim: Quantify IgG/IgM anti-A/anti-B ABO-Abs by Luminex mean fluorescence intensity (MFI) using glycan-functionalized beads and compare MFIs to HA titres.

Methods

We developed ABO single antigen beads (ABO-A and -B subtype I-VI glycans coupled to Luminex beads). Sera from 119 healthy adults were tested for IgG and IgM anti-A and/or anti-B ABO-Abs by Luminex assay. HA was performed using serially diluted sera (50uL) incubated with 25uL of 1% A1 or B erythrocytes; HA titre determined by the last dilution with agglutination.

Results

A wide pattern of increasing median MFIs vs HA titres was evident for IgM ABO-Abs. IgG ABO Abs showed no agreement between MFI and HA titre. A wide range of MFIs was detected at each HA titre for both IgM and IgG anti-A and anti-B ABO-Abs. Levels of one isotype antibody did not predict levels of other isotype antibodies. No significant sex-based differences were detected.

Conclusion

These results demonstrate that HA titre alone is insufficient for accurate ABOi transplant risk assessment. Each HA titre includes an unpredictable range of IgG/IgM ABO-Abs. Titre thresholds alone may unnecessarily deny patients access to ABOi transplants. In contrast, Luminex bead-based ABO-Ab assay will allow more accurate ABOi transplant risk assessment and inform the relative contributions of IgG and IgM isotype ABO-Abs.

Abstracts - In-person Posters

Transmission of Cytomegalovirus (CMV) from CMV Seropositive Organ donors to CMV Seronegative Pediatric Solid Organ Transplant (SOT) Recipients

Geraldine Huynh[1,2], Curtis Mabilangan[1,2], Jutta Preiksaitis[1,3], Catherine Burton[1,3]
1. University of Alberta
2. Department of Pediatrics, University of Alberta
3. Department of Medicine, University of Alberta

BACKGROUND
Rates and risk factors for CMV transmission in CMV-seronegative pediatric SOT recipients (R-) receiving organs from CMV-seropositive donors (D+) in the era of routine antiviral prophylaxis are unknown.

METHODS
Donor-derived CMV transmission, defined as positive CMV PCR and/or CMV seroconversion in a recipient by 2 years post-transplant, and relevant donor and recipient demographics were studied in CMV mismatched (CMV D+/R-) children (<17 years) who had SOT at the Stollery Children's Hospital January 2000-December 2018. Multivariable Cox regression was performed to ascertain effects of organ transplanted, and donor and recipient age and sex, on donor-derived CMV transmission. RESULTS Data from 105 CMV D+/R- pediatric SOT recipients (37% thoracic, 46% liver and 17% kidney) was analyzed. Donor-derived CMV transmission occurred in 58% of CMV D+/R- recipients. Frequency of transmission was highest in liver (73%) then kidney (61%) and lowest in thoracic transplant recipients (39%). Median years to CMV transmission was 0.36 (IQR 0.18-0.56) for liver, 0.39 (IQR 0.31-0.79) for kidney and 0.47 (IQR 0.39-0.70) for thoracic recipients. In multivariate analysis, thoracic and kidney recipients had significantly less CMV transmission than liver recipients (HR 0.32, 95% CI [0.16-0.62], p=0.001; HR 0.43, 95% CI[0.19-.98], p=0.04). Increasing recipient age was associated with increased CMV transmission (HR 1.07, 95% CI [1.01-1.13], p=0.02), but donor age, sex and recipient sex were not

CONCLUSION
Risk of donor-derived CMV transmission is higher in CMV D+/R- pediatric liver recipients than thoracic or kidney recipients. Understanding risk factors for CMV transmission may guide use of antiviral prophylaxis in pediatric SOT recipients.

Abstracts - In-person Posters

EMPOWER – Online mind-body wellness programming for organ recipients aged 50+: A prospective three-armed randomized controlled trial to improve mental health outcomes

Emily Johnson, MSc [1], Puneeta Tandon [1]
(On behalf of all remaining EMPOWER investigators)

1. Division of Gastroenterology (Liver Unit), Department of Medicine, University of Alberta, Edmonton

Background
Organ recipients experience high rates of mental health symptoms, including anxiety and depression, and reduced quality of life. Mind-body wellness programming, including movement, meditation, and psychology practices offer potential treatment solutions but it is unclear how much support is required to promote adherence and effectiveness. In this 3-armed RCT, we will assess the impact of a 12-week online wellness program (EMPOWER) offered at 2 levels of support on the primary outcome of anxiety and depression.

Methods
As part of the larger trial which is recruiting participants across a range of chronic conditions, a tailored program has been developed for post-transplant participants. Inclusion: 50+, transplant ≥6 months ago, no uncontrolled psychiatric symptoms. Random assignment to waitlist control or one of two treatment arms: (1) online program or (2) online program + weekly brief online check-ins with the study team. Each week participants navigate through (a) a clinician tip video, (b) guided mind-body video routines at 4 difficulty levels, and (c) psychology topics based on Acceptance and Commitment Therapy. Mixed methods will be used to assess behavioral drivers and secondary/exploratory outcomes including quality of life, sleep, demoralization, frailty, and acceptability.

Results
The study started March 2023 with recruitment supported through a multimodal strategy including the Canadian Donation and Transplantation Research Program.

Conclusions
There is a high prevalence of mental health symptoms in organ recipients. Once complete, the EMPOWER program will offer evidence of the impact and acceptability of a patient and clinician co-developed program in organ recipients who are 50+.

Abstracts - In-person Posters

Biological Features of Muscle in Patients with Cirrhosis Receiving Liver Transplantation

Maryam Motamedrad [1], Maryam Ebadi [2], Elora Rider [2], Abha-Dunichand Hoedl [1], David Bigam [2], James Shapiro [3], Khaled Dajani [3], Blair Anderson [3], Norman M Kneteman [3], Norberto Sanchez-Fernandez [3], Vickie E Baracos [4], Vera Mazurak [1*], Aldo J. Montano-Loza [2*]

1. Division of Human Nutrition, University of Alberta, Edmonton, AB
2. Division of Gastroenterology and Liver Unit, University of Alberta Hospital, Edmonton, AB
3. Division of Transplantation, Department of Surgery, University of Alberta Hospital, Edmonton, AB
4. Department of Oncology, Cross Cancer Institute, Edmonton, AB

* Denotes co-senior authors.

Background

Sarcopenia is a prevalent condition in patients with cirrhosis and increases risk of death. Whether sarcopenia is modifiable is not known and requires understanding of the underlying biology of muscle loss. This study aimed to further understand the association between sarcopenia, muscle biological features, and impact on patients undergoing LT.

Methods

Biopsies of the rectus abdominis muscle were taken from the surgical incision site at the time of LT from 48 patients with cirrhosis (29 males; 19 females). Muscle fiber types, size, and centralized nuclei (CN) were assessed by immunohistochemistry in serial sections of muscle. Triglyceride (TG) content of biopsies was quantified by gas chromatography. These biological features of muscle were aligned with the quantity of muscle determined by cross-sectional CT or MRI images at the 3rd lumbar vertebra which were taken within 6 months before LT as part of standard clinical assessments. Sarcopenia was defined as L3 SMI <39 cm2/m2 for women and <50 cm2/m2 for men.

Results

The prevalence of sarcopenia was 44% and 52% in males and females, respectively. Males had significantly larger type I muscle fibers (Median; 3625.0 vs. 2354.9 µm2, p=0.007) and more CN compared to females (11.0 % vs. 6.0 %, p=0.007). Fiber type IIA were larger in non-sarcopenic patients compared to sarcopenic patients (Median; 4175.1 vs. 3418.2 µm2, p<0.053). TG content was higher in non-sarcopenic compared to sarcopenic females (39.8±20.9 vs. 21.4±8.2 µg/g, p=0.023) but was not significantly different in male groups.

Conclusion

Sarcopenia in cirrhosis is associated with differences in fiber size.

Abstracts - In-person Posters

Efficacy of Video Telemonitoring to Prevent Adverse Events in Hospitalized Patients with Respiratory Failure on High Flow Oxygen

Jasmine Rai[1], Leann Shewchuk[2], Nicole Zahara[2], Krissa Sidoroff[2], Yvonne Suranyi[2], Jimmy Qiu[3], Ron Damant[1], Marijana Zubrinic[3], Shaf Keshavjee[3], Alim Hirji[1]

1. University of Alberta, Edmonton, AB
2. Alberta Health Services, Edmonton, AB
3. University Health Network (UHN), Toronto, ON

Rationale

After several fatal outcomes due to inadvertent removal of oxygen delivery devices, a video telemonitoring program was instituted at the University of Alberta Hospital, in collaboration with the University Health Network, to monitor inpatients admitted to the pulmonary unit requiring high flow oxygen overnight and to assess if telemonitoring reduced the incidence of falls, ICU admissions, and death on the unit.

Methods

A portable telemonitoring device provided real time video feed of patients on greater than 6L supplemental oxygen or acute non-invasive ventilation, and their vitals to a telemonitoring attendant and to the nursing station during the hours of 10:00 PM-7:00 AM. Patient outcomes including falls, ICU transfers, deaths, and other patient safety events were collected prospectively on the unit. 5-point Likert scale surveys were conducted to gauge patient, caregiver, and health professionals' experience with the telemonitoring system.

Results

In total, 121 patients were monitored between November 2021 and September 2022, for 6180 hours. During this period, there were 813 audio interventions to patients by telemonitoring attendants and 963 calls from telemonitoring attendants to the nurse (mean 2.9x/night). Significant events detected during telemonitoring hours included 146 instances of inadvertent O2 removal and 788 desaturation events ($SpO2 \leq 86\%$).12 falls occurred on the unit in the 9 months prior to telemonitoring while only 3 overnight falls occurred after telemonitoring was instituted (75% reduction).10 ICU transfers and 42 deaths occurred in patients who were not telemonitored during the study period, while 3 ICU transfers and 1 expected death occurred during telemonitoring hours. Overall, patients, caregivers and healthcare professionals (n=38) reported that they had a positive experience with the telemonitoring system, and 100% agreed or strongly agreed that telemonitoring improved quality of care on the unit.

Conclusions

The telemonitoring system allowed staff to intervene in instances of oxygen desaturations and inadvertent oxygen removals, with low rates of ICU transfers, falls and deaths in patients who were telemonitored, and led to enhanced satisfaction by patients, caregivers and health care workers.

Abstracts - In-person Posters

A Model Including Standardized Weight Improved Predicting Waiting List Mortality in Adolescent Liver Transplant Candidates

Abdel Aziz Shaheen[1] , Steven R. Martin[2] , Sahar Khorsheed [2], Juan G Abraldes [3] (presenting author)

1. Division of Gastroenterology and Hepatology, Department of Medicine, University of Calgary
2. Divisions of Gastroenterology and Nutrition, Department of Pediatrics, University of Calgary
3. Division of Gastroenterology, Liver Unit, University of Alberta

Background and Aims
The model of end-stage liver disease (MELD) score has been employed to identify liver transplantation in adolescents since 2004. The current allocation system is proposing MELD 3.0 for adolescent candidates by adding 1.33 points to both male and female adolescent patients. In our study, we follow a recent request from the Organ Procurement and Transplantation Network (OPTN) to evaluate liver transplantation allocation models among adolescents.

Methods
We conducted a retrospective cohort study using data from the OPTN Standard Transplant Analysis and Research (STAR) to identify adolescent patients registered on the liver transplant waiting list in the United States between January 1, 2003 and December 31, 2015. Adolescents (12-17 years) who were listed for their first liver transplantation were included. We evaluated the performance of different models including pediatric end-stage liver disease with Na and Creatinine (PELD-Na-Cr), MELD, and MELD 3.0. Furthermore, we evaluated whether adding anthropometric variables (z-score for weight and height) would improve the models' performance for our primary outcome (mortality at 90 days post-listing).

Results
We have identified 946 eligible adolescent patients. Adding z-score of weight (MELD-TEEN) improved the performance and discrimination of MELD score (c-statistic 0.876). Therefore, the final model including weight z-score (MELD-TEEN) had better discriminative power compared to MELD 3.0 and PELD-Na-Cr in the overall cohort, high MELD scores (≥ 20) and in different age groups (age 12-14 and 15-17).

Conclusion
MELD-TEEN could improve the accuracy of allocation of liver transplant among adolescents by incorporating weight z-score compared to MELD 3.0 and PELD-Na-Cr.

Abstracts - In-person Posters

Perioperative respiratory viruses and primary graft dysfunction risk in lung transplant recipients

Laura van den Bosch [1], Karina Kaur [1], Rhea Varughese [1], Alim Hirji [1], Jason Weatherald [1], Justin Weinkauf [1], Dale Lien [1], Carlos Cervera Alvarez [1], Karen Doucette [1], Dima Kabbani [1], Kieran Halloran [1]

1. Department of Medicine, University of Alberta, Edmonton, Canada

Background

Primary graft dysfunction (PGD) is a form of immediate post-transplant acute lung injury associated with increased risk of mortality. The risk associated with respiratory viruses (RV) at the time of transplant is unknown. We sought to evaluate the association of perioperative RV with PGD.

Methods

We reviewed all adult lung transplant recipients transplanted in our program from 2017-2020. Our primary outcome of interest was grade 3 PGD (PGD3), defined as pulmonary edema on chest x-ray and a PaO2/FiO2 ratio at 48 or 72 hours post-transplant. RV status was assessed as nucleic acid amplification test positive on routine bronchoscopic specimens performed on day one post transplant, and reported as RV+, RV-, or unknown. We used chi square tests and logistic regression to evaluate the association between RV status and PGD3.

Results

259 patients met criteria for inclusion. 33 patients (12.7%) developed PGD3 at 48- or 72-hours. 63 patients (24.3%) were RV+ at time of transplant, while 30 patients (11.6%) were unknown; these were treated as RV-. The majority of RV+ patients had rhino enterovirus (67%). The rate of PGD3 did not differ based on RV status (12.7% RV+ vs. 12.8% RV-; p=1.0). RV+ was not associated with a difference in PGD3 risk adjusted for donor age, use of CPB, or BMI (odds ratio 0.94 [95% confidence interval 0.36-2.27; p=0.9024]).

Conclusion

Perioperative RV were not associated with a difference in the risk of PGD3 in our cohort. This may have implications for donor and recipient selection and preoperative evaluation.

Abstracts - In-person Posters

Optimizing resuscitation of the donation after circulatory death (DCD) heart by pharmacological postconditioning in ex vivo perfused porcine hearts

Fulin Wang [1], Phing-How Lou [1], Eliana Lucchinetti [2], Darren H. Freed [3], Michael Zaugg [1,2]

1. Department of Pharmacology, University of Alberta, Edmonton, AB
2. Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB
3. Department of Surgery, University of Alberta, Edmonton, AB., Canada

Introduction

Heart transplantation remains the gold standard for many cardiovascular diseases, but it is limited by the pool of usable donor hearts. Donation after circulatory death (DCD) hearts are an attractive source of "extended criteria donor hearts", but they suffer significant ischemia-reperfusion injury (IRI) due to the circulatory death process. Intralipid, sevoflurane and remifentanil are well-characterized postconditioning agents known to be cardioprotective and to reduce IRI. Here we investigated the effects of combined pharmacological postconditioning using Intralipid, sevoflurane, and remifentanil during prolonged ex vivo heart perfusion (EVHP) of DCD porcine hearts.

Methods

Porcine DCD hearts were mounted on a custom EVHP apparatus and perfused for 6 hours (n=5-6 per group). Treated hearts were perfused with 1% Intralipid, 2% (v/v) sevoflurane and 3 nM remifentanil, and control hearts were perfused with no postconditioning agents. Heart function parameters were evaluated every hour. Perfusate samples were collected for extracellular vesicle analysis using next generation RNA sequencing. Tissue biopsies were collected at the end of reperfusion for biochemical analyses.

Results

Treated hearts had higher cardiac index (CI) compared to control hearts starting from 2 h (16.52 mL·min-1·g heart weight-1 vs 12.77 mL·min-1·g heart weight-1, P=0.04). In addition, treated hearts had higher left ventricular stroke work (LVSW) starting from 3 h (1576 mmHg·mL-1 vs 790 mmHg·mL-1, P=0.010). Improved heart function persisted in treated hearts until the end of 6 hours of EVHP.

Conclusions

The combination of postconditioning with Intralipid, sevoflurane and remifentanil markedly improved heart function in porcine DCD hearts undergoing 6 h EVHP.

Thanks to the Organizing Committee

ATI Management Team:
Saeideh Davoodi
Patricia Gongal
Diana Tertzakian
Sean Delaney

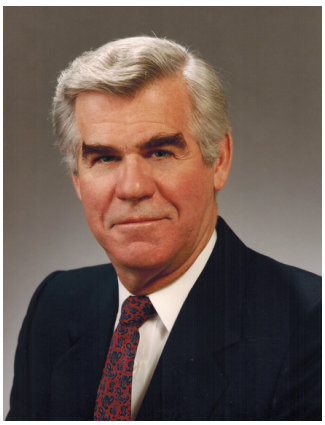
ATI Research Committee (and Session/Poster Judges):
Jason Acker
Esme Dijke
Braulio Marfil Garza
Kieran Halloran
Allan Murray
Lindsey Kemp
Michael Khoury
Andrew Masoud
Gina Rayat

Partners

ATI Research Day is possible only through the support of our partners:

astellas

paladin
une compagnie de endo international
an endo international company



William H. Lakey

Transplantation Lectureship Fund

The Dr William H Lakey Transplantation Lectureship was created through the generosity of the Lakey family. Dr Bill Lakey performed the first kidney transplant at the University of Alberta Hospital in 1967 and would go on to perform nearly 800 more. Dr Lakey was a true transplantation pioneer who bettered the lives of countless Canadians through his passion and dedication.

UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY

Get involved with ATI

Become a member

ALBERTA TRANSPLANT INSTITUTE

Join here

Receive our weekly newsletter

The Transplant Times

Subscribe here

Watch the Seminar Series

YouTube

Follow us on Twitter @AB_OTDT

Give to the Alberta Transplant Institute

Read more about giving options