Maurice McGregor
CARDIOVASCULAR
RESEARCH DAY

Thursday, May 27, 2021
8:30 a.m. - 2:30 p.m.

Organizing Committee

Dr. Negareh Mousavi, Co-Chair
Dr. Jonathan Afilalo, Co-Chair
Dr. Michael Goldfarb
Ms. Giorgina Ciavarella
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Judging Panel

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Dr. Jamie Engert
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Dr. Christopher Labos
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Our sincere thanks to our judges for their expertise in scoring all the abstracts submitted

Table of Contents

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McGill University Heath Centre – Research Institute
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Program

Thursday, May 27, 2021

8:30 - 8:40	Introduction	**Negareh Mousavi, MD MHSc**
8:40 - 8:45	Opening Remarks	**Ernesto L. Schiffrin, CM, MD, PhD, FRSC, FRCPC, FACP, FAHA** Physician-in-Chief, Department of Medicine, Jewish General Hospital Director, Hypertension and Vascular Research Unit, Lady Davis Institute for Medical Research Distinguished James McGill Professor and Vice-Chair (Research), Department of Medicine, McGill University
8:45 - 10:15	Oral Presentations - Session #1 *Moderator*: Negareh Mousavi, MD MHSc	**8:45 - Diana Di Iorio:** The Role of Sex Hormones in Plaque Instability in Men and Women with Carotid Disease **9:00 - Rosie Fountotos:** Prognostic Value of Handgrip Strength in Older Adults Undergoing Cardiac Surgery **9:15 - Ahmad Mahmoud:** Role of Vγ6+ γδ T Cells in Angiotensin II-Induced Hypertension and Vascular Injury **9:30 - Justin Miron:** Exome-Wide Association Study Identifies Rare Protein-Coding Variants for Aortic Stenosis **9:45 - Amir Razaghizad:** Validation of the Thrombolysis in Myocardial Infarction Risk Score for Heart Failure in Diabetes (TRS-HFDM) in Patients with Recent Acute Coronary Syndrome: An Analysis of the EXAMINE Trial **10:00 - Carlos-Eduardo Guerrero-Chalela:** Severe Fontan Associated Liver Disease and its Association with Mortality
	Break	
10:30 - 12:00	Oral Presentations - Session #2 *Moderator*: Ariane Marelli MD, MPH, FRCPC, FACC, FAHA	**10:30 - Sabin Filimon:** A Meta-analysis of Short-term Mortality Rate Among White and Black Women with Acute Coronary Syndrome

		10:45 - Punnanee Wutthigate: Echocardiographic markers in early postnatal life to predict intervention in coarctation of aorta **11:00 - Ida Derish:** Amniotic Mesenchymal Stem Cell Spheroid-Derived Secretome as a Cell-Free Therapy to Improve Angiogenesis in Cardiovascular Repair **11:15 - Iulia Iatan:** A Clinically Validated Genetic Screening for Familial Hypercholesterolemia in Québec **11:30 - Amanpreet Kaur:** Role of Genetics in Differences on Sex specific Effects of Clopidogrel **11:45 - Katerina Eyre:** The Clinical Utility of a Novel, Multi-parametric, Contrast-Free CMR Imaging Technique to Acquire Tissue Characterization Properties
12:00 - 1:00	**Nanette K. Wenger, MD, MACC, MACP, FAHA** Professor of Medicine (Cardiology) Emory University School of Medicine Consultant, Emory Heart & Vascular Center Founding Consultant, Emory Women's Heart Center Atlanta, Georgia	**Understanding the Journey: The Past, Present and Future of CVD in Women** Learning Objectives 1. Understand the journey about CVD in women. 2. Know the advances in provision of information about CVD in women in the past decade. 3. Know the knowledge gaps and research agenda to provide optimal CV care for women.
1:00 - 2:00	Poster Presentations - Session #3 *Finalists*	1:00 - **Pouria Alipour:** Sex, Gender Factors and Cardiovascular Health in Canadian and Austrian populations 1:10 - **Fayeza Ahmad:** Initial Experience of the TARGET-EFT Trial in Frail and Pre-Frail Cardiovascular Inpatients 1:20 - **Kevin Comeau:** The Role of Memory Gamma Delta T Cells in Hypertension and Vascular Damage 1:30 - **Katherine Lindsay:** Value of Deep Learning (ESPIRiT) for Improving the Subjective Quality of Highly Undersampled Cine CMR Images

		1:40 - **Karina Gasbarrino:** Circulating Total Adiponectin is Strongly Associated with Increased Cholesterol Efflux Capacity in Patients with Severe Carotid Atherosclerosis 1:50 - **Isabella Bozzo:** Mechanical characterization of the dynamics of human aortas on a mock-circulatory loop
2:00 - 2:15	Awards:	Awards will be announced by Michael Goldfarb, MD MSc
2:15 - 2:30	Closing remarks	**Ariane Marelli MD, MPH, FRCPC, FACC, FAHA** Professor of Medicine, McGill University Founder, McGill Adult Unit for Congenital Heart Disease Director of Research and Academic Affairs Cardiology, McGill University Health Center

Keynote Speaker

Nanette K. Wenger, MD, MACC, MACP, FAHA
Professor of Medicine (Cardiology)
Emory University School of Medicine
Consultant, Emory Heart & Vascular Center
Founding Consultant, Emory Women's Heart Center
Atlanta, Georgia

Dr. Wenger is Professor of Medicine in the Division of Cardiology at the Emory University School of Medicine and a consultant to the **Emory Heart and Vascular Center.**

Coronary heart disease in women is one of Dr. Wenger's major clinical and research interests. She chaired the U.S. National Heart, Lung, and Blood Institute Conference on Cardiovascular Health and Disease in Women. Dr. Wenger has expertise in cardiac rehabilitation. She chaired the World Health Organization Expert Committee on Rehabilitation after Cardiovascular Disease, and co-chaired the Guideline Panel on Cardiac Rehabilitation for the U.S. Agency for Health Care Policy and Research. Dr. Wenger has had a longstanding interest in geriatric cardiology, is a Past President of the Society of Geriatric Cardiology and was Editor-in-Chief of the American Journal of Geriatric Cardiology for more than 15 years.

Dr. Wenger received the Outstanding Professional Achievement Award from Hunter College (1993), and the Physician of the Year Award of the American Heart Association (1998). In 1999, Dr. Wenger received the Distinguished Achievement Award from the Scientific Councils of the American Heart Association and its Women in Cardiology

Mentoring Award. She was chosen by Atlanta Women in Law and Medicine for Shining Star Award recognizing her distinguished career in cardiology and women's health issues.

In 2000, Dr Wenger was presented the James D. Bruce Memorial Award of the American College of Physicians for distinguished contributions in preventive medicine (2000). In 2002 she received the Distinguished Fellow Award of the Society of Geriatric Cardiology. In 2003, she was included in the National Library of Medicine Exhibition Changing the Face of Medicine: A History of American Women Physicians. Dr. Wenger received the Gold Heart Award, the highest award of the American Heart Association (2004).

At the Emory University 2004 Commencement, Dr. Wenger received the Emory Williams Distinguished Teaching Award of the University and the Evangeline Papageorge Alumni Teaching Award of the Emory University School of Medicine. Dr. Wenger was selected to deliver the 2004 Laennec Lecture of the American Heart Association. In 2006, Dr. Wenger received the Hatter Award, international recognition for the advancement of cardiovascular science. The Georgia Chapter of the American College of Cardiology presented Dr. Wenger its Lifetime Achievement Award in 2009. She was selected Georgia Woman of the Year for 2010. In 2011, Dr. Wenger was selected to deliver the James B. Herrick lecture by the American Heart Association for her outstanding achievement in clinical cardiology. She was elected a member of Emory's 175 Historymakers during Emory's first 175 years.

In 2012, Dr. Wenger received the Charles R. Hatcher, Jr., MD, Award for Excellence in Public Health from Emory University; and was honored in 2013 by the establishment of the J. Willis Hurst, R. Bruce Logue, and Nanette K. Wenger Cardiovascular Society for Emory Cardiology Trainee Alumni. In 2013, she received the Inaugural Distinguished Mentor Award of the American College of Cardiology and the Arnall Patz Lifetime Achievement Award of the Emory University School of Medicine Medical Alumni Association. The American Society of Preventive Cardiology honored Dr. Wenger by naming an annual Nanette K. Wenger Distinguished Lecture focusing on cardiovascular prevention in women (2014).

In 2015, she was awarded the Inaugural Bernadine Healy Leadership in Women's CV Disease Distinguished Award, American College of Cardiology.

Dr. Wenger has participated as an author of several American College of Cardiology/American Heart Association Clinical Practice Guidelines. She is past Chair, Board of Directors, Society for Women's Health Research. Dr. Wenger serves on the editorial boards of numerous professional journals and is a sought after lecturer for issues related to heart disease in women, heart disease in the elderly, cardiac rehabilitation, coronary prevention, and contemporary cardiac care. She is listed in Best Doctors in America.

Dr. Wenger has authored or coauthored over 1500 scientific and review articles and book chapters.

Abstracts for Oral Presentations

The Role of Sex Hormones in Plaque Instability in Men and Women with Carotid Disease

Diana Di Iorio[1], Karina Gasbarrino[1], Huaien Zheng[1], Stella Daskalopoulou[1]

[1]Vascular Health Unit, Research Institute of McGill University Health Centre, Department of Medicine, Faculty of Medicine, McGill University

Background: Carotid atherosclerotic plaques can be stable or unstable; the latter more likely to rupture resulting in strokes. Men develop more unstable carotid plaques than women, yet women have increased mortality rates post-stroke. Sex hormones influence the vasculature differently in men and women; until menopause estrogen protects women against cardiovascular disease. We hypothesize that sex hormones and their receptors may affect plaque instability. Herein, we investigated the role of sex hormones in the circulation and in the plaque of men and postmenopausal women with carotid atherosclerosis who underwent a carotid endarterectomy.

Methods: We developed a liquid chromatography mass spectrometry method to measure circulating testosterone, estradiol, androstenedione, and dehydroepiandrosterone in pre-surgical fasting blood samples from patients undergoing a carotid endarterectomy. Plaques were collected post-operatively and classified into 4 groups (n=20/group): women stable/unstable and men stable/unstable. Immunohistochemistry was performed on plaques to quantify the mean percent area stained for estrogen receptor alpha (ER-a), estrogen receptor beta (ER-b), G protein-coupled estrogen receptor, and androgen receptor (AR). Receptor mRNA expressions were assessed using qRT-PCR.

Results: Although testosterone was significantly higher in men than women, there were no other differences in circulating sex hormone levels across stability/instability in the two sexes. However, men had significantly greater ER-a, ER-b, and AR expression, as assessed by mean percent area of immunohistochemical staining, in unstable vs stable plaques ($p<0.05$), as well as greater ER-a, ER-b, and AR staining compared to women ($p<0.05$). Expression was observed in macrophages, foam cells, endothelial cells, and smooth muscle cells. No differences in ER-a, ER-b, and GPER mRNA expression were detected between participants' groups; however, unstable plaques in men demonstrated significantly less AR mRNA expression compared to stable plaques ($p<0.05$) and compared to women irrespective of plaque type ($p<0.05$).

Conclusion: Our preliminary findings indicate a possible association between sex hormone receptor expression and plaque instability. With further investigations, our ongoing work may ultimately lead to hormone-specific therapies aimed at stabilizing plaques and reducing the incidence of stroke for men and women.

Prognostic Value of Handgrip Strength in Older Adults Undergoing Cardiac Surgery

Rosie Fountotos[1, 2], Haroon Munir[1, 2], Michael Goldfarb[3], Sandra Lauck[4], Kim Dae[5], Louis Perrault[6], Rakesh Arora[7], Emmanuel Moss[8], Lawrence G. Rudski[3], Melissa Bendayan[1, 2], Paulina Piankova[1, 2], Victoria Hayman[2], Julia Rodighiero[2], Marie-Claude Ouimet[9], Sarah Lantagne[2], Nicolo Piazza[10], Jonathan Afilalo[1, 2, 3, 9]

[1]Division of Experimental Medicine, McGill University, [2]Centre for Clinical Epidemiology, Jewish General Hospital, [3]Division of Cardiology, Jewish General Hospital, McGill University, [4]Division of Cardiology, St. Paul's Hospital, University of British Columbia, [5]Division of Geriatric Medicine, Beth Israel Deaconess Medical Centre, Harvard University, [6]Division of Cardiac Surgery, Montreal Heart Institute, University of Montreal, [7]Division of Cardiac Surgery, St. Boniface Hospital, University of Manitoba, [8]Division of Cardiac Surgery, Jewish General Hospital, McGill University, [9]Research Institute, McGill University Health Centre, [10]Division of Cardiology, McGill University Health Centre

Background: While multi-factorial frailty scales have been proven to predict mortality and morbidity in cardiac surgery, there is a need for rapid screening tests that can be easily administered in clinical care settings. Handgrip strength (HGS) is an attractive option because it can be measured in almost all patients, including those that are acutely ill and bedbound, although it has yet to be validated in a large cardiac surgery cohort.

Methods: The prospective McGill Frailty Registry and Frailty-AVR Study was analyzed to determine the association between HGS and outcomes in older patients that had undergone coronary artery bypass and/or heart valve surgery between 2011 and 2019. HGS was measured before surgery using a Jamar dynamometer. Weak HGS was classified based on published sex-stratified cutoffs. Outcomes of interest were all-cause mortality at 1 year and 30 days, discharge disposition, and prolonged length of stay (≥14 days after surgery). Logistic regression models were adjusted for age, sex, body mass index, cardiac and noncardiac comorbidities, surgical procedure and urgency.

Results: The cohort consisted of 1,245 patients with a mean age of 74.0 ± 6.6 years and HGS of 35.9 ± 8.6 kg in men and 20.4 ± 5.8 kg in women. Weak HGS was associated with advanced age, heart failure, kidney disease, anemia, malnutrition, and various frailty scales. In those with weak vs. normal HGS, 1-year mortality was 17% vs. 6%, 30-day mortality was 10% vs. 3%, prolonged length of stay was 19.7 vs. 11.4 days, and discharge to facilities was 45% vs. 26% ($P < 0.001$ for all). After adjustment, weak HGS was predictive of 1-year and 30-day mortality, with odds ratios of 2.44 (CI 1.39, 4.29) and 2.83 (CI 1.38, 5.81), respectively. The cutoff of <26 kg in men and <16 kg in women had higher predictive performance when compared to other published cutoffs.

Conclusions: HGS may be efficiently measured before cardiac surgery to help identify patients at higher risk of mortality and protracted recovery. Older adults with weak HGS may, in turn, benefit from comprehensive geriatric assessment and intervention.

ROLE OF Vγ6+ γδ T CELLS IN ANGIOTENSIN II-INDUCED HYPERTENSION AND VASCULAR INJURY

Ahmad Mahmoud[1], Antoine Caillon[1], Pierre Paradis[1], Ernesto Schiffrin[2]

[1]Hypertension and Vascular Research Unit, Lady Davis Institute for Medical Research, McGill University , [2]Hypertension and Vascular Research Unit, Lady Davis Institute for Medical Research, and Department of Medicine, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montreal, Quebec, Canada

Background: We previously demonstrated that a small subpopulation of T cells considered "innate-like", expressing the gd T-cell receptor (TCR) plays a key role in hypertension and vascular injury. γδ T cells can be subdivided according to the TCR variant (V) subtype that is generally specific for a tissue. A subpopulation of lung and skin γδ T cells that are Vγ6+ and produce interleukin (IL)-17A was shown to respond promptly to pneumococcal infection and skin inflammation. However, γδ T cell Vγ subtypes involved in hypertension are still unknown. We hypothesized that Vγ6+ γδ T cells may play a role in angiotensin (Ang) II-induced hypertension.

Methods: Eleven-to-13-week old C57BL/6J male mice were infused or not with Ang II (490 ng/kg/min, SC) for 14 days and injected IP with control isotype IgG1 or anti-TCR Vγ6 antibodies. Blood pressure was determined by telemetry, mesenteric artery (MA) endothelial function by pressurized myography and T-cell profiling by flow cytometry.

Results: In spleen and mesenteric lymph nodes the most abundant γδ T cells Vγ were Vγ1/2+ and Vγ4+ followed by Vγ6+, Vγ5+ and Vγ7+. In thoracic aortic (TA) perivascular adipose tissue (PVAT), the most abundant γδ T cell Vγ was Vγ6+ followed by Vγ4+, Vγ1/2+, Vγ5+ and Vγ7+. InMA PVAT, the most abundant γδ T cell Vγ subtype was Vγ6+ followed by Vγ4+, Vγ7+, Vγ5+ andVγ1/2+. Ang II increased the frequency of Vγ6+ γδ T cells in the spleen (1.5-fold, $P<0.01$) and TAPVAT (1.6-fold, $P<0.01$), whereas it only tended to increase them in MA PVAT. The frequency ofIL-17 producing effector memory (CCR6+CXCR3–CD44+CD69+) Vγ6+ γδ T cells was increasedin spleen (1.7-fold, $P<0.01$) and tended to be elevated in MA PVAT in Ang II-infused mice compared to control mice. Anti-TCR Vγ6 antibody injections in Ang II-infused mice enhanced theearly elevation of the systolic and diastolic BP ($P<0.05$), and reduced the MA dilatory response toacetylcholine by 50% compared to the control antibody injections ($P<0.05$).

Conclusion: Vγ6+ γδ T cells play a protective role in Ang II-induced hypertension and vascular injury.

Exome-Wide Association Study Identifies Rare Protein-Coding Variants for Aortic Stenosis

Justin Miron[1, 2], Hao Yu Chen[1, 2], Elby Mackenzie[2], Line Dufresne[2], James C. Engert[1, 2, 3], George Thanassoulis[1, 2]

[1]Division of Experimental Medicine, McGill University, Montréal, Québec, Canada, [2]Preventive and Genomic Cardiology, McGill University Health Centre and Research Institute, Montréal, Québec, Canada, [3]Department of Human Genetics, McGill University, Montréal, Québec, Canada

Background: Aortic stenosis (AS) is the leading cause of valvular heart disease in the developed world. Apart from replacement of the aortic valve, there is currently no treatment for this disease. Over the last decade, more than a dozen genetic variants have been identified for AS. However, in addition to being common and non-coding, most of these polymorphisms have small effect sizes. Rare and non-synonymous coding variants may have stronger effects, so identifying these variants could highlight new genes and pathways.

Method: Exome sequence data from more than 200,000 UK Biobank participants were available for an exome-wide association study for AS. We performed an association study using logistic regression adjusted for age, age squared, sex, and the first 20 principal components of ancestry. We analyzed 614,714 exonic variants from 99,888 unrelated White British individuals aged 55 years or older (1,328 AS cases). Functional annotation scoring was performed for genome-wide significant variants ($p < 5.0\times10\text{-}8$) using the Combined Annotation Dependent Depletion (CADD) algorithm.

Results: Sixteen rare (minor allele frequency < 0.0005) and independent variants with large effect sizes (odds ratio [OR] > 13.9) reached genome-wide significance for AS. Among these, eight were intronic and six were missense, while the two remaining were a deletion and a synonymous mutation. Five of the missense variants had CADD scores > 13 (indicating that they are in the top 5% most deleterious variants in the genome) and were in the following genes: *SLIT1* (p.Thr978Ile; OR = 45.0; $p = 3.2\times10\text{-}9$), *OR6S1* (p.Arg264Gln; OR = 24.2; $p = 5.4\times10\text{-}9$), *CCDC85C* (p.Ala32Val; OR = 13.9; $p = 6.7\times10\text{-}9$), *IGDCC4* (p.Pro1123Leu; OR = 40.0; $p = 2.1\times10\text{-}8$), and *SGSM2* (p.Asp415Asn; OR = 87.1; $p = 4.5\times10\text{-}8$). When we used a suggestive p-value threshold of $1.0\times10\text{-}8$, two additional rare (minor allele frequency < 0.00005) and independent missense variants with large effect sizes had CADD scores > 13 and were in the following genes: *CBX1* (p.Asp28Asn; OR = 225.7; $p = 7.2\times10\text{-}8$) and *ZNF717* (p.Gln630Pro; OR = 52.6; $p = 7.9\times10\text{-}8$).

Conclusion: The discovery of rare and non-synonymous variants in *SLIT1*, *OR6S1*, *CCDC85C*, *IGDCC4*, *SGSM2*, *CBX1*, and *ZNF717* identifies new genes for AS. These loci should be explored further as potential therapeutic targets.

Validation of the Thrombolysis in Myocardial Infection Risk Score for Heart Failure in Diabetes (TRS-HFDM) in Patients with Recent Acute Coronary Syndrome: An Analysisof the EXAMINE Trial

Amir Razaghizad[1], João Pedro Ferreira[2], Jiayi Ni[1], Faiez Zannad[2], Abhinav Sharma[1]

[1]McGill University, [2] Université de Lorraine

Background: Assessment of cardiovascular risk is critical for guiding the selection of preventive therapies in patients with type 2 diabetes mellitus (T2DM). The Thrombolysis in Myocardial Infarction Risk Score for Heart Failure in Diabetes (TRS-HFDM) predicts heart failure hospitalization and identifies patients who may derive the most benefit from sodium-glucose cotransporter-2 inhibitors. This study was designed to assess its performance in a high-risk cohort of patients with established cardiovascular disease.

Methods: The Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care (EXAMINE) trial was a randomized, double-blind, multicenter trial in T2DM patients presenting with recent acute coronary syndrome. EXAMINE consisted of 5,380 patients enrolled across 898 centers in 49 countries available for analysis and external validation. Clinical variables in the TRS-HFDM included the history of heart failure (2 points), atrial fibrillation (1 point) and coronary artery disease (1 point), and estimated glomerular filtration rate (<60 mL/min/1.73 m2, 1 point) and urine albumin-to-creatinine ratio (>300 mg/g, 2 points; 30-300 mg/g, 1 point). Model performance was evaluated through discrimination (i.e., Harrell's concordance index) and calibration (i.e., comparison of predicted versus observed outcome probabilities) for the primary composite endpoint of cardiovascular death or heart failure hospitalization.

Results: The mean age of participants was 61 (± 10) years and a primary endpoint occurred in 402 patients. All patients also had an indication of coronary artery disease. Accordingly, 25% of patients were judged as intermediate risk (1 point), 30% were judged as high risk (2 points), 19% were judged as very-high risk (3 points), and 26% were judged as severe risk (≥ 4 points). The TRS-HFDM- demonstrated a strong graded association with the incidence of events. The incidence for cardiovascular death or hospitalization for heart failure ranged between 1.40 to 11.82 cases per 100 person-years for individuals judged at intermediate- and severe-risk, respectively. Discrimination was robust for the primary endpoint, with the concordance index equaling 0.72. Calibration was mostly modest, with the calibration-in-the-large and calibration slopes ranging between -0.25 and -0.13 and 0.82 and 0.74 for 6- and 30-month event predictions, respectively. However, model performance was superior for the secondary endpoint hospitalization for heart failure alone (concordance index = 0.75).

Conclusion: The TRS-HFDM robustly predicts and stratifies for heart failure specific outcomes in patients with T2DM and established cardiovascular disease, supporting its use for clinical decision making and cardiovascular risk assessment. Implementation of the TRS-HFDM may improve patient outcomes and health service utilization.

Severe Fondan Associated Liver Disease and its Association with Mortality

Carlos Guerrero-Chalela[1], Therrien Judith[1], Liming Guo[1], Aihua Liu[1], Ariane Marelli[1]

[1]MAUDE Unit

Background: Fontan-associated liver disease (FALD) is a major extracardiac complication in Fontan patients. Data is scant in the incidence of severe FALD and its association with mortality. The objectives of this study are threefold: 1) estimate the cumulative probability of developing severe FALD in patients with Fontan and compare to patients with Ventricular septal defect (VSD); 2) assess the association between severe FALD and mortality 3) identify risk factors for developing severe FALD.

Methods: Using the Quebec Congenital Heart Disease Database, Fontan patients surviving longer than 30 days post-Fontan were identified, and each matched to 20 VSD patients on birth year and sex. Severe FALD was defined as at least one hospitalization due to liver disease. Kaplan-Meier curve analysis was used to illustrate the cumulative probability of severe FALD in the Fontan-VSD cohort. Within Fontan patients, severe FALD patients were matched to non-FALD patients on selected comorbidities to assess the association between FALD and mortality using Kaplan-Meier curve analyses and Cox proportional hazard models. Another Cox proportional hazard model was built among Fontan patients to identify risk factors for severe FALD development.

Results: A total of 512 Fontan patients and 10,232 VSD patients were included. Of the Fontan patients, 98 (19.14 %) developed severe FALD at the median age of 15.3 (IQR: 4.8, 23.3). The cumulative risk of developing severe FALD in Fontan patients was 11.95% and 52.24% at 10 and 35 years, much higher than 0.50% and 2.75% for the VSD cohort (LogRank p<0.0001). At five years, the cumulative risk of death was 12.60% in patients with severe FALD vs 3.70% in patients without FALD (LogRank p=0.0171). Congestive heart failure (CHF) and supraventricular tachycardia (SVT) were strongly associated with the development of severe FALD with HRs of 2.3 (95% CI: 1.38, 4.02) and 2.4 (95% CI: 1.37, 4.39), respectively. More recent Fontan completion was related to reduced risks of severe FALD with an HR of 0.9 (95% CI 0.93-0.97) for each more recent year.

Conclusions: Fontan patients are at high risk for severe FALD and then mortality. Conditions that promote poor Fontan hemodynamics, including CHF and SVT, were risk factors for severe FALD. A recent calendar year of Fontan completion was associated with decreased risk of severe FALD, suggesting a longer exposure to Fontan physiology as a hazard to develop severe FALD. Studies are needed to understand the trajectory leading to severe FALD and mortality.

A Meta-analysis of Shosrt-term Mortality Rate Among White and Black Women with Acute Coronary Syndrome

Sabin Filimon[1]

[1]McGill University - Division of Cardiology

Background: It remains unclear whether black and white women with acute coronary syndromes (ACS) have similar short-term mortality. We completed a meta-analysis comparing short-term mortality of black to white women with ACS.

Methods: We searched nine databases from January 1st 1987 to February 27th, 2020 . We only retained studies which reported short-term mortality for both black and white women (up to 30-days including in-hospital mortality). We completed random-effect meta-analyses andmeta-regression by SAS version 9.4.

Results: There were 13 studies which reported short-term mortality for 213,940 black women and 2,289,055 white women with ACS. The mean age was 65.4 years (95% CI; 61.7 to 69.1), 69.9 years (95% CI; 66.7 to 73.1) for black and white women, respectively. The weighted mean prevalence and 95% confidence intervals for diabetes mellitus (DM) and hypertension (HTN) were 46.3% (95% CI; 43.6 to 48.9), 84.5% (95% CI; 79.9 to 88.1), and 28.9 % (95% CI; 25.9 to 32.1), 69.8% (95% CI; 62.4 to 76.3) for black and white women, respectively. Invasive revascularization either by percutaneous coronary intervention or coronary artery bypass graft was done in 71.1% (95% CI; 25.3 to 94.7) of black women and 82% (95% CI; 35.4 to 97.4) of white women. Adjusted for age, DM, HTN and invasive revascularization there was no conclusive difference in short-term mortality (OR 1.53; CI 0.62 to 3.78).

Conclusion: Black women with ACS have more DM and HTN compared to white women. Even though they were younger, black women have similar short-term mortality as white women with ACS. More intensive control of diabetes mellitus and hypertension may further improve the prognosis of black women with ACS.

Echocardiographic markers in early postnatal life to predict intervention in coarctation of aorta.

Punnanee Wutthigate[1], Jessica Simoneau[1], Gabriel Altit[1], Claudia Renaud[1]

[1]Montreal Children's Hospital, Mcgill University

Background: Coarctation of the aorta (CoA) is challenging to diagnose in the prenatal and early neonatal life due to the patent ductus arteriosus (PDA). The aim of this study was to describe the resource utilization, the early post-natal cardiac profile and the predictors for the need of cardiac surgery in those with antenatal suspicion of CoA.

Methods: Retrospective single-center study of infants with an antenatal suspicion of CoA, without major associated cardiac anomalies, and born at ≥37 weeks between January 2014 and March 2020. The analyzed echocardiography (ECHO) was performed within 48 hours after birth. Those not requiring post-natal intervention (normal group) were compared to those that required post-natal cardiac surgery (CoA). Data extractors were masked to the outcome.

Results: A total of 51 newborns were included, of which 40 (78%) were considered with an adequate post-natal arch and 11 (22%) underwent intervention. There was no difference on baseline characteristics for groups (gestational age, sex and mode of delivery). In the normal group, median hospitalization was 4 [2-6] days, and 6 (15%) were exposed to prostaglandin E (PGE) infusion (100% in CoA group). Also, 38 of the normal group (95%) were started on intravenous fluids, 9 (23%) required gavage and median age at full feeds was 3 days (IQR: 2-5). There was no difference on physical exam at admission between both groups (absence of femoral pulses and differential in saturations or blood pressure). On first post-natal ECHO (day 1 [1-2]), PDA was patent in all newborns and aortic measurements were smaller in the CoA group: ascending aorta diameter (0.76 [0.12] *vs* 0.65 [0.12]; p=0.01), proximal transverse arch (0.58 [0.10] *vs* 0.38 [0.08] cm; p <0.001), distal transverse arch (0.48 [0.09] *vs* 0.33 [0.07] cm; p<0.001), and aortic isthmus (AI) (0.36 [0.07] *vs* 0.26 [0.07] cm; p<0.001). Post-natal right ventricular predominance was significantly higher in the CoA group, as demonstrated by the left ventricular end-systolic eccentricity index (EI) (1.60 [0.28] *vs* 2.16 [0.45]; p<0.001). AI and EI were highly predictive for later intervention (OR 26, 95%CI (-42 to -9); p=0.002, OR 4.5, 95%CI (1.5-7.5); p=0.003).

Conclusions: Majority of those with antenatal suspicion of CoA did not require intervention but were consumers of numerous medically related resources. Despite PDA patency, AI and EI on first post-natal ECHO were predictors for later need for intervention.

Amniotic Mesenchymal Stem Cell Spheroid-Derived Secretome as a Cell-Free Therapy to Improve Angiogenesis inCardiovascular Repair

Ida Derish[1], Kashif Khan[1], Renzo Cecere[1, 2]

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Background: A myocardial infarction (MI) is caused by an obstruction of the coronary arteries of the heart, resulting in necrosis and maladaptive cardiac remodelling. The terminally differentiated cardiomyocytes and cardiac vascular cells are unable to repair the damaged myocardium. Consequences of this pathophysiology often manifest as heart failure in surviving patients, an irreversible cardiovascular disease with no curative therapies available. Over the past 20 years, stem cells have been studied due to their regenerative potential, but trials have yielded insufficient cell engraftment post-injection as well as unreliable differentiation into cardiac cells. We examined a novel cell-free strategy utilizing the stem cell secretome, which bypasses the limitations of stem cell injection while improving cardiac function. The secretome contains soluble factors such as proteins, microRNA, long-noncoding RNA, many of which are considered key components in paracrine communication-mediated tissue regeneration and are involved in cell proliferation, angiogenesis and anti-apoptosis.

Methods: We hypothesized that the secretions collected from amniotic stromal mesenchymal stem cell (AMSCs) 3-dimensional spheroids (3D) will upregulate repair-promoting biological processes in human cardiac microvascular endothelial cells (HCECs). To test this hypothesis, we first characterized the AMSCs via immunofluorescence staining of cardiac markers. After treating HCECs with 2D and 3D cell culture-derived secretome, we performed Alamar Blue assays, neovessel formation assays and migration assays.

Results: We found a significant increase of metabolic activity in HCECs treated with 3D-derived secretome, compared to untreated HCEC controls ($p < 0.0001$) and HCECs treated with 2D cell culture-derived secretome. Spheroid-derived secretome caused a higher number of capillary-like HCEC tubules to form ($p < 0.05$). Higher cell migration speed was detected in 3D secretome-treated HCECs ($p < 0.05$) than in 2D secretome-treated HCECs and untreated controls. Expression of prominent cardiac markers connexin 43 (CXN43), sarcoendoplasmic reticulum Ca2+ ATPase (SERCA2a), GATA4 and Troponin T was confirmed in the spheroid ASMC cultures via immunocytochemistry, suggesting their cardiogenic potential.

Conclusions: Altogether, our data suggests that the ASMC spheroids are an advantageous source of angiogenesis-boosting secretome, improving metabolism, blood vessel formation and migration processes of HCECs to a higher degree than the 2D ASMC-derived secretome. Our results highlight the potential of this novel and readily harvestable therapeutic agent for cardiovascular repair, to improve patient outcomes and recuperate healthy heart function.

A Clinically Validated Genetic Screening for Familial Hypercholesterolemia in Québec

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Background: Familial Hypercholesterolemia (FH) is the most common genetic disorder in humans with an estimated prevalence of 1/311. In geographic regions with founder effect mutations, such as the province of Québec, prevalence is as high as 1/80. FH is associated with premature atherosclerotic cardiovascular disease caused by elevated low-density lipoprotein cholesterol (LDL-C). Although early diagnosis and therapy of FH can normalize life expectancy, less than 15% of cases are diagnosed. Cascade screening and genetic testing aim to improve diagnosis, treatment, and outcomes in FH.

Methods: Here, we report a single center experience with the only clinically validated molecular genetic screening for FH (CLIA compliant) in Canada. We performed next generation sequencing of the *LDLR*, *APOB* and *PCSK9* genes and multiplex ligation-dependent probe amplification (MLPA) of the *LDLR gene* to detect genetic mutations and copy number variants. All mutations were reviewed by a geneticist and cross-referenced in ClinVar.

Results: Between 2018-2020, we examined 369 FH cases (57% males, 43% females) based on the Canadian FH definition clinical criteria. For index patients, mean age at diagnosis was 40±16 years, while it was 30±16 years for cascade screening patients. Baseline (untreated) LDL-C was 6.5±2.0 mmol/L. In 224 patients who underwent genetic testing, a pathogenic mutation was identified in 167 (75%) individuals, in keeping with ~20% of FH patients with a polygenic form. A majority of affected patients had mutations in the *LDLR* (87%) or *APOB* (13%) genes. Interestingly, the genetic panel offered by Quebec's Health Ministry, which includes 10 common mutations in French Canadians, only accounted for 46% of identified mutations. Even in patients self-describing as French Canadians, more than 20% did not have a common mutation. We subsequently examined the impact of genetic testing in re-classification of patients' FH diagnosis. There were 3 (1%) individuals with a "severe hypercholesterolemia" phenotype initially categorized as "not FH" and 85 (38%) with "probable FH" re-classified to "definite FH".

Conclusion: Genetic testing in patients suspected of having FH provides diagnostic certainty and permits re-classification of individuals with a diagnosis of "severe hypercholesterolemia" or "probable FH" according to current definitions. Furthermore, the limited genetic panel offered by the province, focusing on common French-Canadian mutations, provides incomplete data in the majority of cases. We therefore propose that most patients with a presumptive diagnosis of FH undergo an unbiased genetic analysis. This study has implications on cascade screening, public health policies and reimbursement of drugs such as PCSK9 inhibitors.

Role of Genetics in Differences on Sex specific Effects of Clopidogrel

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Background: Poorer health outcomes experienced by young women with acute coronary syndrome (ACS) could be related to sex differences in the safety and efficacy of commonly used antiplatelet agents such as clopidogrel. Sex and polymorphisms in drug metabolism enzyme [cytochrome P450 (CYP) family] genes are independent factors for the variability in response to clopidogrel including thrombotic risks. For example, loss of function cytochrome P450 (CYP) alleles confer higher platelet reactivity, which has been associated with a higher incidence of thrombotic events. However, the role of genetics on sex-specific effects to explain worse clinical outcomes in women has not yet been extensively explored.

Methods: We used the GENESIS-PRAXY and VIRGO cohorts of young ACS patients (18-55 years) to identify single nucleotide polymorphisms (SNP) in CYP genes. We explored interactions between sex and genes amongst users of clopidogrel at the time of presentation via a case-only design. A case-control analysis was performed among clopidogrel users at discharge to determine if sex interaction exists between the SNP variants and thrombotic readmission event. A logistic regression to assess the interaction between each SNP and sex among users of clopidogrel at index event was performed.

Results: Among 2,272 patients (56% women), 177 were on clopidogrel at the time of presentation. The case-only analysis showed that thrombotic risk was greater in female carriers of CYP2C9*3 loss-of-function (LOF) allele (OR=3.77, 95% CI=1.54-9.24, p=.003). The results of multivariate logistic regression model for users of clopidogrel at index event (n=1,733) showed that the number of women had significantly higher rate of thrombotic readmissions (OR= 1.55, 95%CI=1.16-2.07) at 1 year as compared to men. The LOF alleles (CYP2C9*3, CYP2C19*2,*4, CYP3A5*2,*3,*6) were not associated with thrombotic readmission.

Conclusion: Loss-of-function allele CYP2C9*3 confers a higher risk of ACS in young women, which is likely explained by a higher on-clopidogrel platelet reactivity. Assessment of emzyme polymorphism involved in drug response could help to better understand risk and benefit of the drug based on patient's sex.

The Clinical Utility of a Novel, Multi-parametric, Contrast-Free CMR Imaging Technique to Acquire Tissue Characterization Properties

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Background: Cardiovascular Magnetic Resonance (CMR) is a versatile imaging modality, providing information on morphology, function, and tissue characteristics [1]. Long scan times and dependence on respiratory and cardiac gating limit CMRs widespread applicability due to patient discomfort and inefficiency. Recently, Multitasking has emerged as a multi-parametric, contrast-free imaging technique which retrospectively resolves cardiac and respiratory motion and T1 recovery [2]. We hypothesize that Multitasking can reduce scan time, without compromising T1 mapping characterization accuracy and image quality.

Methods: Fourteen healthy volunteers (mean age = 43.4) underwent a cardiac MRI exam using both the Multitasking protocol (CINE, T1 and T2 maps) and the standard protocol (bSSFP CINE, MOLLI 5:3:3 T1 and TRUFI T2 maps). All scans took place on the 3T Skyra scanner (SIEMENS, Germany) at the McGill University Health Centre (MUHC) (study number: 2020-6128).

Results: A paired t-test showed no significant differences in global T1 values between the Multitasking (mean = 1208, SD = 119.8) and standard protocol (mean = 1235.1, SD = 43.15). Segmental T1 values between protocols were also comparable except for the mid-apical antero-lateral, inferior, infero-lateral and apical anterior segments ($p < 0.05$). A linear mixed effects model showed that age, HR, BMI, and sex do not significantly confound the differences in global T1 values between protocols. The Multitasking protocol (time = 11±4 mins) was significantly shorter than the standard protocol (time = 25±10 mins) ($p < 0.05$). Significant differences in the average IQ (read by two experienced readers) were found between the Multitasking series and the bSSFP CINE and MOLLI ($p < 0.05$). An ease of use survey conducted by 6 experienced technologists showed that both protocols were user friendly with no inconsistencies. Amongst the respondents, 67% report repeating the standard protocol 2-3 times, whereas only 17% report repeating the Multitasking protocol 2-3 times. On average, the respondents report “rarely/never” seeing significant artefacts while scanning using the Multitasking protocol, while “sometimes” when using the standard protocol. In terms of ease of learning, both protocols were easy to learn and remember, and felt comfortable executing independently.

Conclusion: Multitasking is an easy-to-use, multi-parametric, contrast-free CMR imaging technique with accurate global T1 mapping values and decreased scan times when compared to a standardprotocol. Further studies should seek to optimize IQ and assess the clinical feasibility of Multitasking in a larger patient cohort.

Abstracts for Poster Presentations - Finalists

Sex, Gender Factors and Cardiovascular Health in Canadian and Austrian populations

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Introduction: Little evidence exists differentiating the effect of biological sex from gender-related (i.e. psycho-socio-cultural) characteristics in cardiovascular outcomes. Here, we explored the association between sex, gender, and cardiovascular health (CVH) among Canadians (CAN) and Austrians (AT).

Methods: Data from the Canadian Community Health Survey (CCHS) (n=63,522, 55% Females) and Austrian Health Interview Survey (AT-HIS) (n=15,771, 56% Females), were analyzed. The CANHEART index, a measure of ideal CVH composed of 6 cardiometabolic risk factors ranging from 0 (worst) to 6 (ideal), was calculated in the CCHS as well as AT-HIS databases (ATHEART). A country-specific gender score was computed using principal component analysis-derived propensity score methods. The final gender scores (Range=0-1, higher score identifying characteristics traditionally ascribed to women) included: i) household size, perceived life stress, education level, sense of belonging to community, marital status, and income (CAN); ii) household size, perceived mental health, education level, marital status and income (AT).

Results: Median CANHEART and CAN gender scores were 4 [3-5] and 0.53 [0.49-0.60] while median ATHEART and AT gender scores were 4 [3-5] and 0.55 [0.46-0.64]. Although higher gender scores (CCHS: β=-1.33, 95%CI (-1.44,-1.22); AT-HIS: β=-1.11, 95%CI (-1.30,-0.91)) were associated with worse CVH, female sex (CCHS: β=0.35, 95% CI (0.33,0.37); AT-HIS: β=0.59, 95%CI (0.55,0.64)) was associated with better CVH in both populations in the model adjusted for age. Additionally, higher gender scores were associated with a higher risk of heart disease, compared to female sex. The magnitude of this risk was higher in AT population. (Table1).

Conclusion: Individuals with characteristics typically ascribed to women reported poorer CVH and exhibited higher risk of heart disease independent of biological sex. Gender factors must be targeted for improving cardiovascular health.

Initial Experience of the TARGET-EFT Trial in Frail and Pre-Frail Cardiovascular Inpatients

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Background: Older adults are at risk for hospital-acquired disability and deconditioning, often leading to the "post-hospitalization syndrome" of accelerated functional decline. We hypothesized that this syndrome could be prevented by a pragmatic multi-faceted intervention in patients with acute cardiovascular conditions, and now report the initial experience of our ongoing randomized clinical trial.

Methods: Patients admitted to the cardiovascular ward at a single academic center are screenedwith the Essential Frailty Toolset (EFT). Those ≥65 years with frailty (EFT 3-5) or pre-frailty (EFT1-2) are eligible for the TARGET-EFT trial, in which they are randomly allocated to usual care orintervention. The intervention is targeted such that patients with weakness receive supervised exercise sessions (in addition to clinically-indicated physiotherapy), those with cognitive impairment receive stimulation activities, those with iron deficiency anemia receive intravenous iron sucrose and those with malnutrition-related hypoalbuminemia receive protein supplements. The outcome is a composite score representing mobility, disability, activity, discomfort, and mood(EQ-5D-5L) ascertained by a blinded observer on the day of discharge and at 30 days.

Results: To date, 77 out of a planned 144 patients have been randomized. The most common reasons for exclusion are age <65 years, expected discharge within <3 days and patient refusal. The median age is 80 years and length of stay is 8 days. In each group, 1 patient withdrew and 1 died. There were no intervention-related adverse events. Of the 39 intervention patients, 36 qualified for exercise and received an average of 6 sessions (46% of sessions were deferred because patients were away for tests, were bedrest post-procedures, or refused), 18 received cognitive stimulation, 15 received intravenous iron sucrose, and 16 received protein supplements.

Conclusion: The TARGET-EFT intervention is feasible and appears safe for frail and pre-frail patients hospitalized with acute cardiovascular conditions.

Role of Memory Gamma Delta T Cells in Hypertension and Vascular Damage

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Background: It has been shown that the immune system plays an important role in the pathogenesis and maintenance of hypertension. We demonstrated that γδ T cells, a small subset of immune cells bridging innate and adaptive immunity, participate in the pathogenesis of hypertension. Depleting γδ T cells in mice reduced the ability to induce hypertension and vascular injury via subcutaneous infusion of angiotensin II (Ang II). γδ T cells are unconventional, innate-like T cells that express a γδ T cell receptor (TCR) instead of conventional αβ TCRs, and γδ T cells can respond rapidly to pro-inflammatory cytokines secreted by innate cells. Evidence also suggests that memory T cells may develop during an initial hypertensive episode, sensitizing mice to develop hypertension to further mild hypertensive challenges. Upon an initial exposure to an antigen, a population of memory T cells is established which could then be reactivated upon subsequent interaction with the previously encountered antigen. However, whether memory γδ T cells develop and play a role in hypertension remains unknown. We hypothesize that memory γδ T cells form after an initial exposure to a hypertensive stimulus and that they respond to further mild hypertensive insults, worsening hypertension. Our objective is to determine if memory γδ T cells sensitize mice to develop hypertension in response to a mild hypertensive challenge.

Methods: Ten-12-week-old C57BL/6J mice were exposed or not to a hypertensive challenge (490 ng/kg/min Ang II, SC) for two weeks, followed by a two-week washout period, and then infused with a subpressor dose of Ang II (140 ng/kg/min Ang II, SC) for two weeks. Blood pressure was measured via telemetry and central, effector, and resident memory γδ T cells were profiled by flow cytometry.

Results: Mice exposed to the first hypertensive challenge had a systolic blood pressure ~30 mm Hg higher than the sham group after the subpressor hypertensive challenge (P <0.001). After 14-days of Ang II infusion, effector memory γδ T cells increased 4.5-fold in the mesenteric artery perivascular adipose tissue (PVAT), and 2.4-fold in the mesenteric lymph nodes (mLN) (P<0.05). After repeated Ang II infusion, central memory γδ T cells decreased by 65% in the aortic PVAT, and by 23% in the mLN (P<0.05).

Conclusion: An initial exposure to a hypertensive stimulus sensitizes mice to develop hypertension to a subsequent subpressor hypertensive challenge and results in the development of memory γδ T cells.

Value of Deep Learning (ESPIRiT) for Improving the Subjective Quality of Highly Undersampled Cine CMR Images

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Background: Recent fast image acquisition and reconstruction techniques, typically through undersampling k-space, can significantly shorten Cardiovascular magnetic resonance (CMR) scan times. One of these techniques, variable density spatiotemporal (VD k-t) sampling, shortens image acquisition duration from 5 or more heartbeats (RR) in a gold standard FIESTA Cine technique with ASSET reconstruction ("FIESTA cine"), to 3 or even 1 RR interval, allowing for a short axis stack acquisition during a single-breath hold. A known trade-off to such techniques however is reduced image quality. Novel deep learning (DL) reconstructions, such as DL ESPIRiT, may resolve this, filling in undersampled k-space and thereby improving the perceived image quality. The aim of this study is to assess the image quality of VD k-t images acquired during 3 RR intervals (3rr) or 1 RR interval (1rr), reconstructed with undersampled (k-t ARC 3rr), highly undersampled (k-t ARC 1rr), or DL reconstruction (DL-ESPIRiT), compared to standard cine (FIESTA).

Methods: Eight healthy participants and eight patients were scanned on a 3T GE Premier research scanner. Using a 4-point scale (1=poor, 2=fair, 3=good, 4=excellent) we compared the image quality (IQ) in de-identified images of six combinations of acquisition and reconstruction techniques: standard cine, undersampled cine, highly undersampled cine, and DL reconstruction. Statistical significance was determined using ANOVA tests with multiple comparisons.

Results: All 16 subjects completed the protocol and were included in the analysis. Significant differences in IQ were noted in all comparisons (see Fig. 1). Overall, the IQ of both standard cine and DL reconstruction was superior to the undersampled cines, with standard cine also superior to DL reconstruction. DL reconstructions showed significantly better IQ than both the undersampled (P=0.0015, mean difference= 0.479±0.438) and highly undersampled cine (P< 0.0001, mean difference=0.958 ±0.643). Standard cine showed significantly better IQ than both the undersampled (P< 0.0001, mean difference=0.792 ±0.453) and highly undersampled cine (P< 0.0001, mean difference=1.875±0.698). Lastly, standard cine showed significantly better IQ thanboth the DL reconstruction at 3rr (P=0.0118, mean difference=0.313 ±0.375) and 1rr (P< 0.0001,mean difference=0.917±0.464). The largest difference in IQ was between the standard and highlyundersampled cine, while the standard cine and DL reconstruction at 3rr were the most similar.

Conclusions: Although incompletely, the subjective quality of undersampled cine images can begreatly improved by deep learning algorithms like ESPIRiT to produce diagnostic results.

Circulating Total Adiponectin is Strongly Associated with Increased Cholesterol Efflux Capacity in Patients with Severe Carotid Atherosclerosis

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Background: Cholesterol efflux capacity (CEC) as a measure of HDL functionality is independently associated with increased risk for coronary artery disease (CAD), cardiovascular events, and advanced atherosclerotic plaque morphology. Many factors in the circulation can influence cholesterol efflux. Anti-inflammatory adiponectin, along with proinflammatory chemerin and resistin, are circulating adipokines with direct influence on vascular function. Herein, we investigated the association of CEC with circulating adipokines and evaluated their impact on post-surgical outcomes in patients with severe carotid atherosclerosis.

Methods: Consecutive patients with severe carotid atherosclerosis (≥50% carotid artery stenosis), scheduled for a carotid endarterectomy (CEA), were recruited from McGill-affiliated hospitals. Fasting blood samples were collected pre-operatively to measure plasma total and high-molecular weight [HMW] adiponectin, chemerin, and resistin, and to perform cholesterol efflux assays in J774 macrophage-like cells. Sociodemographic and clinical information, as well as 5-year post-CEA outcomes (any ischemic cerebrovascular event, myocardial infarction, death, restenosis) were obtained through medical chart review.

Results: A total of 285 subjects were included. Subjects had a mean age of 70.1 ± 9.4, were 67.0% male, had various comorbidities (hypercholesterolemia [85.3%], hypertension [83.5%], type 2 diabetes [34.5%], CAD [38.6%]), and previously experienced cerebrovascular symptomatology (77.9%). Univariate linear regression analyses using CEC as a dependent variable demonstrated significant and positive associations with total and HMW adiponectin but no association with chemerin or resistin. Importantly, total adiponectin had the greatest association accounting for 8.3% of the variance in CEC, while HMW adiponectin for only 2.8%. The association between total adiponectin (but not HMW adiponectin) and CEC remained significant following adjustments for age, sex, BMI, comorbidities, symptomatology, plaque stability, carotid artery stenosis, inflammatory and lipid markers, and other adipokines. Interestingly, interaction regression models demonstrated a significant interaction between adiponectin and chemerin in increasing CEC. Notably, with each unit increase in CEC there was a 92.9% decrease in the odds of having an ischemic cerebrovascular event 5 years post-CEA. Following adjustments for circulating adipokine levels, this relationship was significantly strengthened (OR: 0.032; CI: 0.002-0.453).

Conclusions: Circulating adiponectin was independently and positively associated with CEC in patients with severe carotid atherosclerosis. Total adiponectin had the greatest association, suggesting that its lower-molecular weight isoforms may also contribute significantly to increasing CEC. High levels of CEC were significantly associated with reduced odds for an ischemic cerebrovascular event 5 years post-CEA. In subjects with impaired CEC, adiponectin may serve as a potential therapeutic target for raising CEC levels and reducing cardiovascular risk.

Mechanical characterization of the dynamics of human aortas on a mock-circulatory loop

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Background: An increasing interest in cardiovascular surgery is replacing widely used synthetic grafts, like Dacron, with innovative biomaterials or engineering tissues, since Dacron fails to correctly mimic the dynamic behaviour of the aorta. Thus, this has motivated research to better understand the dynamic mechanical properties of the aorta.

Method: A novel mock circulatory loop (MCL) was designed to test donated human thoracic descending aortas obtained from Transplant Québec. The circuit that was developed to simulate physiological pulsatile flow conditions and measure the bending and breathing modes of vibration with laser Doppler vibrometers. From the pressure-displacement relationship, the viscoelastic material properties were determined computationally for the dissipation and compliance of the tissue.

Results: This study presents results obtained for eleven human thoracic aortas tested on the MCL. The results showed cyclic axisymmetric diameter changes, which were comparable to in-vivo measurements at a resting heart rate. An increase of the dynamic stiffness with age was observed. As well, it was noted that with increasing age there was a strong reduction of the cyclic diameter change at resting heart rates, and a significant reduction of the energy dissipation. Larger dissipation was observed at higher pulse rates due to the combined effects of fluid-structure interaction and viscoelasticity of the aortic wall. Overall, when compared with the viscoelastic properties of Dacron, the aortas of even the stiffness donors was much more compliant than Dacron leading to long term increases in afterload following graft surgical repairs.

Conclusion: The projected outcome of this work is to create innovative biomaterials that better reproduce the aortic dynamic behavior. The findings complement expanding avenues in advanced materials, with the aim of creating improved and mechanically compatible cardiovascular devices, like grafts and stents.

Abstracts for Poster Presentations

(listed in order of submission)

Prospective Study of Electrocardiogram Efficiency in the Emergency Department

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Background: The electrocardiogram (ECG) is a crucial tool for the early detection of an acute ST-elevation myocardial infarction (STEMI). It is essential to complete this procedure in a timely matter to decrease the door-to-balloon time. This study aimed to determine the efficiency by assessing which factors delay the process of obtaining an ECG once requested by the physician.

Methods: This was a two-month prospective mixed-methods study at the Jewish General Hospital's Emergency Department (ED). Volunteers directly observed ED nurses performing the ECG, and collected qualitative and quantitative data at each predefined step. The observer timed each distinct step of the ECG protocol using the TimeTag application. The steps started at bringing the ECG machine to the patient's room until showing the ECG to the emergency physician.

Results: Forty-two ECG tests were observed with a median of 393 seconds (sec) per test, and an interquartile range (IQR) of 328–553 sec per test. The median time per step was: 25 sec (IQR: 15–61 sec) for finding and bringing the ECG machine to the patient, 30 sec (IQR: 25–50 sec) for cleaning the cables and machine, 47 sec (IQR: 28–69 sec) for turning on and/or syncing the machine, 117 sec (IQR: 88–176 sec) for prepping the patients and attaching the electrodes, 28 sec (IQR: 21–51 sec) for entering the patient's information into the machine, 54 sec (IQR: 43–76 sec) for acquiring and printing out the ECG and removing the leads from the patient, 28 sec (IQR: 24–41 sec) for cleaning the machine after usage, and 54 sec (IQR: 28–120 sec) for showing the emergency physician the ECG. The most common issues noted by the observers include finding a machine within the ED, the cleaning of the ECG machines prior to usage, and the disentanglement of the ECG lead cables.

Conclusions: The analysis of the data suggests potential proficiency improvements of the ECG procedure. If the overall efficiency of the procedure were to be improved between the 85th to 95th percentile, it would result in a 160 to 197 sec (2.67 to 3.28 minutes) decrease in the length of time. Any saved time by fixing these delays provides an earlier detection of a STEMI and a shorter ischemia time.

Role of Sex and Gender in Access to Care and Cardiovascular Complications of Individuals with Diabetes Mellitus

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Background: The impact of biological sex and social determinants of health (gender) on the prevalence of cardiovascular risk factors such as diabetes mellitus (DM) may vary by culture and health systems. In this study, we aimed to elucidate how sex and gender influence access to care and cardiovascular outcomes of individuals with diabetes mellitus across different countries.

Methods: Data from the Canadian Community Health Survey (CCHS, 2015-16) (N=109,659, 53.7% Females, 8.4% Type 1 or 2 DM) and the European Health Interview Survey (E-HIS) (N=316,333, 51.3% Females, 7.3% Type 1 or 2 DM), were analyzed. A composite measure of socio-cultural gender was constructed. The relationship between the gender score, antihyperglycemic care (Canada: checking HbA1c in the past 12 months, Europe: checking blood sugar in the past 12 months), complications and hospitalization of individuals with DM was assessed with a logistic regression model adjusted for age, sex, body mass index, and comorbidities. European countries were stratified based on their Gender Inequality Index (GII); which quantifies gender disparity and inequity amongst various countries in the world, from low-GII (GII<0.077), to medium (GII: 0.077-0.1635) and high (>=0.1635).

Results: The mean gender score was 0.54 ±0.09 in both populations. Characteristics traditionally ascribe to women (i.e., higher gender score) included greater stress level, being widowed or divorced, larger household size, higher education, good sense of belonging to community, and lower income in Canadians; while being divorced or widowed, having greater household size, lower education and lower income were found in Europeans. Sex and gender significantly influenced the standard care of patients with diabetes including periodic glucose and HbA1C monitoring. Canadian diabetic females were more likely to check their HbA1c (OR: 1.26, 95%CI: 1.01-1.6), while European counterparts were less likely to check their blood sugar (OR: 0.89, 95%CI:0.79-0.99). Additionally, higher gender scores independent of sex were associated with higher risk of heart disease, stroke and hospitalization in all countries albeit European countries with medium to high GII, conferred a higher risk of all complications and hospitalization rates compared to low GII countries (Table1).

Conclusion: Regardless of biological sex, diabetic individuals with characteristics typically ascribed to women and those living in countries with greater gender inequality, exhibited poorer antihyperglycemic care, greater risk of cardiovascular complications, and higher hospitalization rates. Country-specific gender related factors and gender disparity must be targeted for improving health status and access to care of patients with diabetes mellitus.

Impact of an Apolipoprotein B Subset of a Genetic Risk Score for Coronary Artery Disease

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Background: Coronary Artery Disease (CAD) is the leading cause of death worldwide producing a high societal burden. Genome wide association studies have identified many variants, although many of these variants have small effects. However, when these variants are compiled into a genetic risk score (GRS), their sum demonstrates a stronger effect. It may be possible to increase our understanding of CAD etiology by exploring metabolic subsets of GRS.

Methods: A weighted GRS for myocardial infarction (MI) and CAD containing 204 single nucleotide polymorphisms (SNPs) was used to examine the strength of its association with CAD/MI using non-overlapping subsets of SNPs partitioned by their effects on apolipoprotein B (apoB). We subdivided the GRS by selecting genome-wide significant ($P \leq 5 \times 10\text{-}8$) SNPs for apoB plasma levels (GRSapoB; 102 variants) and a subset containing the remaining SNPs (GRSminusApoB; 102 variants). We included 384 674 unrelated White British individuals from UK Biobank in a cross-sectional analysis. These GRS were tested for association with CAD/MI and low-density lipoprotein cholesterol (LDL-C) using logistic regression models adjusted for age and sex. We also examined interactions of the GRS with age, sex, and lipids.

Results: The 204 SNP GRS was associated with CAD/MI (odds ratio (OR) per standard deviation (SD) [95% CI], 1.37 [1.35,1.39]; $P<2\times10\text{-}16$). The GRSapoB (OR per SD [95% CI], 1.27 [1.26,1.29]; $P<2\times10\text{-}16$) and GRSminusApoB (OR per SD [95% CI], 1.22 [1.2,1.24]; $P<2\times10\text{-}16$) were also significantly associated but with reduced effect sizes. The effect on CAD/MI by all three GRS appeared to decrease with age: ORinteraction per SD [95% CI], 0.96 [0.94,0.97], $P = 5.4\times10\text{-}7$; ORinteraction per SD [95% CI], 0.98 [0.96,0.99], $P=0.0066$; and ORinteraction per SD [95% CI], 0.96 [0.94,0.98], $P = 1.2\times10\text{-}5$ for an 8-year increase in age, respectively. The GRSapoB was strongly associated with LDL-C (mmol/L per SD [95% CI], 0.12 [0.12,0.12]; $P <2\times10\text{-}16$) while the GRSminusApoB was much less so (mmol/L per SD [95% CI], 0.0033 [0.00038,0.0061]; $P=0.026$).

Conclusion: Partitioning a CAD/MI GRS by apoB resulted in similar associations with CAD/MI and thus the genetic contribution mediated by apoB to CAD/MI was similar to the contribution of variants that work through other pathways. They both also demonstrated a similar interaction with age with a stronger impact on younger individuals.

Clonal Hematopoiesis of Indeterminate Potential (CHIP) Predisposes to Aortic Stenosis – A Large-Scale Study

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Background: Clonal hematopoiesis of indeterminate potential (CHIP) is a condition characterized by somatic mutations in hematopoietic stem cells leading to the overabundance of specific clonal populations in the bloodstream. The contribution of CHIP to cardiovascular diseases has been little studied. In particular, CHIP's contribution to aortic stenosis (AS), despite it being among the most common and severe valve conditions, has not yet been the subject of a large-scale analysis. The present study assesses the contribution of this emerging risk factor to aortic stenosis.

Methods: The UK Biobank (UKB) and Genetic Epidemiology Research on Adult Health and Aging (GERA) cohorts feature linkage of electronic health record data with genome-wide imputed data in 500 000 and 100 000 participants respectively. After filtering for unrelated individuals of European ancestry aged 55 years or older, a weighted genetic risk score (GRS) was built for the remaining 260 381 (UKB) and 55 192 (GERA) individuals using 23 single-nucleotide polymorphisms (SNPs) recently associated with CHIP. Ages of selected individuals ranged from 55 to 70 in UKB and from 55 to above 90 in GERA. The association of the GRS with AS was separately estimated in each cohort using logistic regression adjusting for age and sex. The results were meta-analyzed using an inverse-variance weighted fixed effects meta-analysis.

Results: In the UKB, the GRS was associated with AS (odds ratio [OR], 1.10; 95% CI, 1.01 to 1.19; p=0.026). The association in GERA was similar when the samples matched the UKB age range but did not reach statistical significance (OR= 1.17; 95% CI, 0.99 to 1.38; p=0.066). The meta-analysis combining these two results was significant and showed no evidence of heterogeneity (OR= 1.11, 95% CI, 1.03 to 1.19; p=5.1 × 10-3, $I2$=0).

Conclusion: Our results confirm an association of genetic susceptibility to CHIP with AS. Future studies will have to investigate the mechanism by which this association occurs.

iPSC Secretome in the Rescue of Cardiomyocytes After Doxorubicin-Induced Injury

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Myocardial infarction (MI) often leads to heart failure or death due to the cardiac tissue's inability to regenerate after injury. Unlike other organs in the human body that have innate reparative capabilities after an injury like the liver, the human heart undergoes maladaptive remodelling after injury and its condition worsens over time. There have been many attempts to implant stem cells and immature cardiac cells into infarcted hearts to try to induce recovery, yielding insignificant results and a lack of cardiac function improvement. Now, the focus has shifted towards cell-free therapies to induce cardiac repair after MI. This study aims to evaluate the secretome of induced pluripotent stem cells (iPSCs) generated from heart failure patients and healthy individuals as a potential treatment for doxorubicin (DOX)-injured primary cardiomyocytes (CMs). The secretome of stem cells contains soluble proteins and extracellular vesicles that are thought to act as paracrine mediators of repair. We hypothesize that the secretome of iPSCs from both diseased patients (SiPSC-DP) and healthy controls (SiPSC-HC) will significantly increase CM metabolic activity and viability, and decrease CM hypertrophy after DOX-induced injury.

CD34+ cells were isolated from diseased patients (n=3) and a control patient's (n=1) blood and reprogrammed into iPSCs using episomal vectors. Stem cells were passaged multiple times (P5-P10) to ensure purity, and their secretome was collected whilst their confluency was at 50%, 75% and 100%. AC16 CMs were treated with 0.5μM of DOX for 24 hours, which has been shown to mimic a heart failure phenotype in CMs by significantly reducing metabolic activity, while significantly increasing cellular hypertrophy and cell death. DOX-injured CMs were treated with i) SiPSC-DP, ii) SiPSC-HC, or iii) mesenchymal stem cell secretome. AlamarBlue, crystal violet, and actin immunostaining assays were conducted to assess changes in CM metabolism, viability, and hypertrophy, after treatment with secretome.

We hope to elucidate whether iPSCs generated from patient blood make an effective source of secretome to treat cardiac tissue after injury. Additionally, we seek to evaluate if the confluency of iPSCs influences the effectiveness of their secretome. Determining the effectiveness of the stem cell secretome from different sources in treating damaged cardiomyocytes will be a step towards the usage of secretome as a cardiac repair therapy. If SiPSC-DP is as effective as SiPSC-HC, then our future direction will be to validate our results on a larger dataset and evaluate the effect of patient-specific iPSC secretome on DOX-injured iPSC-derived cardiomyocytes.

Recurrent Disease Progression Networks for Modelling Risk Trajectory of Heart Failure

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Background: Heart failure (HF) is one of the most important predictors of death among patients with congenital heart disease (CHD). Although the research on heart disease treatment has significantly advanced along with the field of biomedical sciences, the long-term prediction of HF remains illusive. Several types of HF prediction studies focused on readmission and survival for CHD patients. Such evaluation metrics along with the widely used biomarkers such as natriuretic peptides often performed poorly when applied to different cohorts.

Methods: We present a Recurrent neural network (RNN) model called Deep HeartTrajectory Model (DHTM). DHTM models not only the HF trajectory but also the longitudinal data from EHR on age and surgery history as well as inpatient and outpatient diagnosis record. To predict long-trajectory of heart failure, we use the predicted HF at future time point t as an input to the Gated Recurrent Units for predicting the HF at the time point t+1. Furthermore, we propose a second model named as DHTM+C. Here we predict both the HF and comorbidity at time point t and use the predicted HF and CM as input to the recurrent unit in order to predict HF at t+1.

Results: Data source is the Quebec CHD database with 84498 patients and 28 years of follow up (1983 – 2010). We evaluated our proposed models and baseline models on two prediction tasks: (1) next time point prediction; (2) trajectory prediction. For task 1, we used the observed t time points to predict the t+1 time point for each patient, for all of the time points T_p - 1 time points for patient p. For task 2, each RNN model was given 15 years of co-morbidities changes and heart failures, starting from the age of 40. Our DHTM and DHTM+C achieved the highest precision-recall. For task 2, our DHTM+C also conferred much higher recall score than the baseline long-short-term-memory (LSTM) model, even for many years in the future. In particular, both our DHTM models are able to recall 50% of the positive HF events at the first-year trajectory and nearly 20% of the positive HF at year 10. In contrast, LSTM can only recall 5% in year 1 and 1% in year 10.

Conclusion: This is the first study to model the long-term HF trajectories in CHD patients. The DHTM-C achieves the best precision and recall, suggesting the benefits of jointly modeling the trajectory of HF and comorbidities.

Association of LPA Haplotypes with Lipoprotein(a) Concentrations Across Multiple Ethnicities

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Background: Lipoprotein(a) is a particle that is associated with several cardiovascular diseases including coronary artery disease, myocardial infarction, and aortic stenosis. This particle is composed of a low-density lipoprotein-like moiety and an apolipoprotein(a) glycoprotein coded for by the *LPA* gene. Shorter *LPA* isoforms are associated with greater apolipoprotein(a) concentrations and increased cardiovascular disease risk. *LPA* isoform size is determined by a copy number variant known as the Kringle IV type 2 repeats (KIV2). Additionally, the average number of KIV2 repeats and lipoprotein(a) levels are known to vary widely between different ethnicities. There may also be differences in the association between lipoprotein(a) and cardiovascular disease between different ethnicities. Haplotypes, which are collections of variants on the same strand of DNA, may be useful to better understand the link between ethnicity and lipoprotein(a) concentrations.

Method: Putative haplotypes that span the KIV2 repeats in the *LPA* gene were created with the program PLINK and tested for their association with lipoprotein(a) concentrations. Using unrelated individuals from the UK Biobank (UKB) cohort, haplotypes were constructed from fourteen common SNPs (minor allele frequency > 0.30) separately for White British and three other ethnicities: South Asians, Chinese, and Blacks. A subset of four variants out of the fourteen were available from indigenous populations present in the Human Genome Diversity Project (HGDP), including Sub-Saharan Africans, South Asians, East Asians, West Asians, and Native Americans.

Results: Two haplotypes were identified in the *LPA* region that span the KIV2 repeats in White British individuals that account for >99% of the haplotypes. These two *LPA* haplotypes are associated with opposing effects in lipoprotein(a) levels (ß = 0.23, $p < 5 \times 10\text{-}315$; ß = -0.24, $p < 5 \times 10\text{-}315$). These same two haplotypes were also identified, at similar frequencies, in Chinese and South Asian individuals and were associated with lipoprotein(a) levels. Black individuals had a much more heterogenous haplotypic composition.

The *LPA* haplotype frequency is comparable between UKB and HGDP for ethnicities found in both cohorts (average minor haplotype frequency difference = 0.083). HGDP Native Americans and West Asians also demonstrate similar haplotype frequencies to non-African ethnicities across both cohorts. The haplotype frequencies in Sub-Saharan Africans are less heterogenous than UKB Africans.

Conclusions: A kringle repeat spanning *LPA* haplotype is associated with lipoprotein(a) concentrations and has been highly conserved in many populations.

Future work should assess if this *LPA* haplotype is also associated with specific ranges of KIV2 repeat numbers.

Agile software development methodology as a key success for the development of the "READYorNot" e-Health Intervention --- READiness in Youth fOR traNsition Out of pediaTric care

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Background: Lifespan conditions are increasing in prevalence as children survive to adulthood with chronic diseases such as brain-based disabilities (BBD). Transition from pediatric to adult care is a resource-intense and complex process that needs to engage health systems, patients, families, and intersectoral pediatric and adult care providers. Despite guideline recommendations that transition of care should be anchored to structured processes, few programs exist. There is thus a growing need for health interventions that bridge care between pediatric and adult providers by providing a Health Information Technology (HIT) solution.

Method: A multidisciplinary collaboration —engaging thought leadership in clinical psychology, translational medicine, BBD, as well as patient and families' insights— was initiated to design, develop, and clinically validate the MyREADY Transition BBDTM, an e-Health intervention, to educate and empower young adolescents as they undergo on this transition from pediatric to adult care.
In order to ensure that the e-Health intervention can respond to stakeholder needs, particularly the adolescent users; there was a need to incorporate them on the HIT development process which included the creation and validation of the HIT components such as the interface design and the content of the mobile and desktop applications.
Agile software development methods were used to incorporate patients, families and researchers' feedback during the development of the HIT tool. This methodology, focused on flexibility, adapts to changing user requirements and facilitates user acceptance and project success.
The READYorNotTM intervention gaming approach is presented as a Journey in the City where a Mentor helps the user navigate through 19 educational sections containing videos and skill-based-achievement challenges along the six-week training curriculum.
The MyREADY TransitionTM BBD App is available on Apple Store and Google Play for participants in the randomized control trial. Due to the challenging circumstances of COVID-19, the team is conducting a pilot on a controlled environment in order to validate the technical support and training procedures and adapt the recruitment to the pandemic.

Conclusions: The MyREADY TransitionTM BBD App intervention is expected to improve quality of care and patient and family experiences during transition with a potential for reduction in cost that is expected to be translatable across pediatric and adult health care systems. Our findings are also expected to inform guidelines and policy recommendations for a growing number of patients with childhood conditions requiring life-long care; integrate family members and care givers or incorporate a community platform for all parties' participation in the future.

Opportunistic Biomarkers of Frailty from CT Imaging in Patients with Suspected COVID-19

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[1]McGill University, [2]Lady Davis Institute

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Background: Frailty is more meaningful than chronological age for risk prediction and patient-centered decision making in COVID-19. While frailty scales may be challenging to use in this setting, computed tomography (CT) scans are often performed and provide access to opportunistic biomarkers of frailty such as skeletal muscle area (SMA).

Methods: We conducted a cohort study nested in the prospective Quebec COVID-19 Biobank. Symptomatic patients presenting to our acute care hospital were eligible if they underwent a COVID-19 test and a clinically-indicated CT scan of the chest or abdomen. Using the CoreSlicer web-based software, we loaded CT images and measured SMA and subcutaneous fat area at 3 pre-defined axial levels (T6, T12, L4). The current analysis focuses on scans acquired in the first 24 hours and on images at the T6 level; if not included in the scan field, multiple imputation was used based on the closest available level. The primary outcome was log-transformed hospital length of stay.

Results: Out of 770 patients included in the Biobank at our hospital, 232 met the inclusion criteria. At the T6 level in men and women, respectively, the mean SMA was 140±37 cm2 and 99±26 cm2 and the mean subcutaneous fat area was 135±67 cm2 and 217±133 cm2. SMA was inversely correlated with Rockwood's Clinical Frailty Scale (Spearman R -0.43, P<0.001). In the linear regression model adjusted for age, sex, Charlson comorbidity index, and COVID-19 status, lower SMA was independently associated with prolonged length of stay (Beta -0.018, 95%CI -0.001 to -0.035).

Conclusion: CT-based measures of muscle and fat area were reliably feasible in 97% of scans. Patients with suspected COVID-19 and low muscle mass on clinical CT scans had higher risks of adverse in-hospital outcomes.

Assessing adherence to the 2017 Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery at Saint Mary's Hospital

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Background: This retrospective observational study assesses adherence to the 2017 Canadian Cardiovascular Society Guidelines at Saint Mary's Hospital (SMH)1. Specifically, this study investigates perioperative cardiac risk assessment and management of patients who underwent elective non-cardiac surgery at SMH. Perioperative cardiac risk is measured using the Revised Cardiac Risk Index. Studying adherence to recommended medical guidelines in a pre-operative setting helps to determine the relationship between clinical assessment and patient outcomes.

Methods: A retrospective chart review was performed. The study population consisted of patients aged 65 and older who were discharged from St. Mary's after having elective non-cardiac surgery between January 1st, 2018 to April 30th, 2019. Patients included in the population had: 1 overnight stay at the hospital post-operatively and had undergone an assessment in SMH's pre-op clinic.

Results: We analyzed peri-operative clinic compliance rates with the 2017 Canadian Cardiovascular Society Guidelines for 49 patients. Our results show that compliance rate with RCRI calculation *documented* was 8.2%. Compliance rate in accordance with ordering BNP was 49%, and of those ordered 20% were elevated (BNP ³ 92). 18% of participants had troponins ordered post-op with 0 positive; however of those ordered, only 44% were ordered appropriately when BNP ³ 92. Of the 31% of patients who took aspirin or anticoagulants, 94% had it *clearly documented* that their medication was discontinued ³ 48h pre-operatively. Additionally, only 8% of patients had a pre-operative stress test or echocardiogram.

Conclusion: Of our patient population, only 8.2% had their RCRI clearly documented in the pre-operative clinic. It is likely that the RCRI was calculated by the physician, but without clear documentation we were unable to account for this. It is also of note that not all patients had a BNP ordered, despite guidelines stating that anyone 65 and over should have one done. Furthermore, only 44% of troponins post-operatively were appropriately ordered. In terms of pre-operative stress testing and echocardiograms, there is no evidence of unnecessary testing.

We suggest implementing a RCRI checklist in the pre-operative clinic to facilitate clear documentation of cardiovascular risk. Additionally, a BNP should be an automatic order for any patient undergoing elective surgery who is > 64 years old. Some of these changes are already being implemented in the peri-operative clinic. However, further study is needed to assess compliance with the 2017 guidelines, and we suggest performing another study to evaluate the impact of the institutional changes in the peri-operative clinic.

Reassessing the Benchmark: An Analysis of Time Delays and Complications in the Management of Carotid Endarterectomy Patients

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Background: Fatal strokes are generally preceded by milder ischemic episodes such as amaurosis fugax or transient ischemic attacks. Acknowledging the risk of severe stroke is greatest shortly after symptom onset, early surgical intervention—via carotid endarterectomy (CEA)—is desirable. According to the American Heart Association and the Society of Vascular Surgery, CEA is indicated in recently symptomatic patients with stenosis ≥50% and asymptomatic individuals with stenosis ≥60%. Current stroke prevention guidelines recommend the time delay between symptom onset and CEA be kept to at most 14 days. However, in clinical practice, this guideline is not necessarily met, and ensuing complications can be deadly. This study served to assess: how often the 14-day standard is met; where delays are occurring; sex differences in delays; and effects of meeting the benchmark on post-CEA outcomes.

Methods: From a population of 600 patients who underwent CEA at McGill University affiliated hospitals, a sample of 181 patients who were operated on between March 2015 and November 2018 was included in this study. Retrospective chart review enabled pertinent clinical characteristics, medications, post-CEA outcomes and dates and timing of symptom onset, surgery, first medical contact (FMC), relevant imaging and diagnostic tests to be noted. Patients were then stratified into groups based on sex and symptom status, and baseline characteristics, presenting symptoms, timings, and post-CEA outcomes were compared.

Results: When stratified based on sex and symptom status, significant patient characteristics were age, degree of carotid stenosis and supportive imaging, with asymptomatic patients having higher degree of stenosis and less imaging. The 14-day benchmark was met in 18.3% of cases, with a median time from symptom to surgery of 41.5 days. Significance was seen for the timing between FMC and surgery, and imaging and surgery. Post-hoc analysis revealed the source of this difference was between symptomatic and asymptomatic individuals with greater delays among asymptomatic patients, independent of sex. Seeing as the time between FMC and imaging was not significant, the true source of delay was the time between imaging and surgery. Finally, meeting the 2-week benchmark did not significantly affect post-CEA outcomes.

Conclusion: This study confirmed the 14-day benchmark from symptom onset to CEA is rarely met. However, surgical delays appear to be sex independent and to not significantly affect post-operative outcomes. Further analysis of time delays showed more significant delays among asymptomatic vs. symptomatic individuals, with the main source of delay attributable to the time between imaging and surgery.

Echocardiographic Quadriceps Muscle Thickness: A Practical Biomarker for Frailty

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Background: Sarcopenia and physical frailty have been shown to be risk factors for mortality and major morbidity in older adults suffering from various forms of cardiovascular disease. Ultrasound measurement of quadriceps muscle thickness (QMT) is an emerging biomarker for sarcopenia, which we hypothesized could be conveniently acquired during the routine echocardiographic exam. The objective of our study was to demonstrate the feasibility of measuring QMT at the time of echocardiography, and determine the association between QMT and clinical indicators of frailty.

Methods: Adult inpatients and outpatients undergoing a clinically-indicated echocardiogram for known or suspected cardiovascular disease were recruited for this cross-sectional study at the Jewish General Hospital. Prior to the echocardiogram, trained research assistants measured height, weight, and three clinical indicators of frailty: Rockwood's Clinical Frailty Scale, handgrip strength (Jamar dynamometer), and bioimpedance phase angle (InBody 770). At the conclusion of the echocardiogram, cardiac sonographers blinded to the preceding assessments acquired a biplane image of the anterior thigh midway between the anterior superior iliac spine and knee, and measured QMT as the combined thickness of the rectus femoris and vastus intermedius muscles. A cardiac ultrasound machine and probe were used (GE Vivid E9, 1.5-4.5 MHz probe).

Results: The cohort consisted of 301 patients, of which 290 had an available measure of QMT. The acquisition and measurement of QMT added 1-2 minutes to the echocardiographic exam. The mean age was 65±15 years with 56% females. The mean QMT was 30±9 mm, similar in men and women, with the lowest quintile being <22.2 mm. Higher age and lower body mass index were associated with lower QMT. After adjustment for age, sex, and body mass index, QMT was found to be associated with the multivariate composite of frailty indicators (P<0.001), particularly with the Clinical Frailty Scale (Beta -0.03 per mm; CI -0.04, -0.01) and bioimpedance phase angle (Beta 0.02 per mm; CI 0.01, 0.03). Additional adjustment for heart failure and inpatient status did not alter results.

Conclusions: QMT can be efficiently measured during a routine echocardiographic exam and can add incremental insights about frailty in a diverse group of patients with cardiovascular disease.

Health-Related Quality of Life in Older Adults with Acute Cardiovascular Disease Undergoing Early Mobilization

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Background: Post-hospitalization syndrome occurs commonly in older adults following critical illness. Early mobilization during hospitalization has been shown to be safe and feasible in older adults with acute cardiovascular disease and may improve post-hospitalization patient-centred outcomes. Our objective was to assess post-hospitalization health-related quality of life (HRQOL) in older adults with acute cardiovascular disease undergoing early mobilization.

Methods: Patients aged ≥60 years admitted to the cardiovascular intensive care unit were prospectively enrolled at the Jewish General Hospital, an academic tertiary care centre in Montreal, Quebec, from January 2018 to January 2020. Patients participated in a structured, bedside early mobilization program consisting of functional level-specific mobilization activities beginning as soon as hemodynamic stabilization was achieved. Functional status was measured using the Level of Function Mobility Scale to guide twice-daily level-specific mobility activities. HRQOL was measured using the Short-Form 36 (SF-36) questionnaire administered by telephone at 1 and 12-months post-hospital discharge. The primary outcome was SF-36 physical component summary (PCS) score 1-month post-hospitalization. A difference in PCS of 3 points is considered the minimal clinically important difference. Secondary outcomes were PCS at 12-months and mental component summary (MCS) scores at 1- and 12-months. Results were compared to a published Canadian normative dataset for SF-36 scores.

Results: There were 147 were patients included in the analysis (75.0 ± 8.7 years old; 44.6% female; 48.6% with ischemic heart disease). The mean 1-month PCS score for patients was 34.7± 9.7 . The PCS score at 1-month was 11.5 points lower and 8.4 points lower compared to age-matched Canadian normative data for people aged between 65-74 years old and ≥75 years old, respectively. The mean PCS score was 36.5 ± 9.2 at 12-months and the mean MCS score was 36.9 ± 11.1 at 1-month and 40.5 ± 11.5 at 12-months, all of which were significantly lower than normative data ($P<0.0001$). In the multivariable analysis, increased age and worse prehospital functional status were associated with lower PCS at 1-month.

Conclusions: Older adults with acute cardiovascular disease had lower HRQOL at 1- and 12-months post-hospitalization than age-matched Canadian norms. Prehospital functional status was predictive of poor post-hospitalization HRQOL. Future studies are needed to determine whether EM in older adults can improve post-hospitalization patient-centred outcomes, particularly in older adults with poor prehospital functional status.

Effect of In Vitro Fertilization on Arterial Stiffness and Hemodynamics Throughout Pregnancy: An Analysis of the REVEAL Study

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Background: In vitro fertilization (IVF), a form of assisted reproductive technology, is a risk factor for the development of hypertensive disorders of pregnancy. At the time of embryo transfer, IVF has also been associated with increased maternal arterial stiffness (AS), which is a composite indicator of cardiovascular health. To better understand the impact of IVF on vascular health during pregnancy, AS and hemodynamic parameters of women who conceived by IVF were compared to those who conceived naturally.

Methods: Existing data from 235 pregnant women with singleton pregnancies recruited in high-risk obstetrical clinics for the REVEAL study, that aimed to assess whether AS can predict hypertensive disorders of pregnancy, were analyzed. AS and central hemodynamics were measured via applanation tonometry every 4 weeks from 10 to 41 weeks gestation. Brachial blood pressure measurements were acquired using an automated oscillometric blood pressure monitor. Angiogenic biomarker levels of PlGF and sFlt-1 were measured at each trimester and 6 weeks postpartum. Linear regression models were used to evaluate differences in AS throughout pregnancy between those who conceived through IVF or spontaneously after adjustment for gestational age, heart rate, body mass index and mean arterial pressure.

Results: Baseline characteristics were similar between both groups. Unadjusted analyses showed that the IVF group had higher central systolic blood pressure (SBP) by 5.0 mmHg (95% CI 0.3-9.6) and peripheral SBP by 5.9 mmHg (95% CI 1.0-10.8) during the 380-416 week period than those who have conceived spontaneously, albeit within normal limits. Only differences in peripheral SBP remained significant in adjusted analyses. No differences were noted in the other AS parameters or in the incidence of complications of pregnancy. Anti-angiogenic marker sFlt-1's levels were higher by 164.50 pg/mL (95% CI 54.8-274.2) in the IVF group than the spontaneously conceiving group during the 2nd trimester.

Conclusion: Significant differences in sFlt-1 levels and peripheral SBP were noted in the 2nd and 3rd trimester, respectively. However, IVF treatment did not influence central AS/hemodynamic parameters in our cohort and was not associated with the development of complications of pregnancy.

Sex as a Barrier to Care in Familial Hypercholesterolemia

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Background: Familial hypercholesterolemia (FH) is an inherited condition characterized by elevated low-density lipoprotein cholesterol (LDL-C) in the blood. If left untreated, FH leads to the development of premature atherosclerotic cardiovascular disease (ASCVD) and death. Many barriers to care in FH exist, which can result in low rates of diagnosis and suboptimal treatment and outcomes. Sex disparities have been identified as an important barrier to care in CVD, however their influence on treatment, lipid target achievement and CVD outcomes in FH remains to be explored.

Methods: Here we performed a longitudinal registry analysis of sex differences in treatment and lipid level achievement in Heterozygous FH (HeFH) patients at the MUHC. Patients were included in the study if they were diagnosed as either “definite”, “probable”, or “possible” FH based on the Simon-Broome criteria, Dutch Lipid Clinic Network criteria, or the new Canadian FH definition. Differences between women and men were calculated using a *t*-test or chi-squared test.

Results: 127 women and 162 men from the McGill FH Registry were included in the analysis. The mean age at the initial clinic visit was 49±17 years for women and 45±16 years for men (p=0.04). First, we analyzed sex differences in lipid lowering medication use. At the most recent clinic visit, there were more men (89%) than women (76%) taking statins (p=0.7), and only 35% of women were on high-intensity statins, compared to 74% of men (p=0.002). Interestingly, statin intolerance was reported in 40% of women and 22% of men (p=0.02). We then examined guideline-recommended lipid target achievement between both sexes. At baseline, men and women had similar mean LDL-C levels of 6.9±2.2 mmol/L and 6.7±1.6 mmol/L respectively (p=0.7). Despite this, at the most recent visit, 55% of men reached a target LDL-C of ≤ 2.5 mmol/L compared to just 32% of women (p=0.02). As well, from baseline to most recent visit, women reduced their LDL-C by 51%, whereas men lowered their LDL-C by 62% (p=0.01). Thus, fewer women are reaching appropriate guideline-based target LDL-C levels compared to men.

Conclusion: Our analysis reveals a sex bias in FH patients in favour of men in regard to treatment intensity and lipid level target achievement. Identifying these imbalances will allow us to break down these barriers in care through educational initiatives and additional training, to improve quality of life and life expectancy of individuals with FH.

Adiponectin accelerate regulation of macrophages lipid metabolism in the process of HDL formation

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Aim: Adiponectin's role in the regulation of macrophage lipid metabolism, a crucial process in atherogenesis, remains poorly investigated. We aim to characterize the adiponectin's role in HDL biogenesis.

Methods and results: We perform kinetics studies in baby hamster kidney (BHK) and Tamm-Horsfall protein 1 (THP-1) cell lines to elucidate adiponectin's role in HDL biogenesis. In cholesterol-enriched cells, specific molar doses of adiponectin stimulated cholesterol efflux with high efficiency to apoA-I. In the presence of adiponectin, BHK cells expressing ATP binding cassette transporter A1 (ABCA1) or ABCG1 generated lipidated particles having α electrophoretic mobility (α-HDL) and a molecular size of 7.5–20 nm. Interestingly, in THP-1 macrophages, cholesterol efflux was associated with more lipidated preβ1-HDL particles. Direct molecular interaction of adiponectin with apoA-I enhanced the affinity of apoA-I to free cholesterol and resulted in an increase in preβ1-HDL particles from human plasma *ex vivo*. Adiponectin increased ABCA1 and ABCG1 protein expression and activated the formation of ABCA1-linked cholesterol oxidase sensitive plasma membrane domains.

Conclusion: Adiponectin promotes efficiently apoA-I/HDL-mediated cholesterol efflux via ABCA1 and ABCG1 respectively, reduced lipid accumulation in cells, and efficiently promoted nascent HDL formation. These results highlight that these cellular processes are interconnected through adiponectin and ABCA1- and ABCG1-dependent. In this pathway, adiponectin increased the affinity of apoA-I to cholesterol and effectively accelerated cholesterol removal from the plasma membrane to HDL particles. Thus, by accelerating and upregulating HDL biogenesis, adiponectin may have therapeutic potential for atherosclerotic cardiovascular disease prevention and management.

Prognostic capabilities of the preoperative six-minute walk test to inform cardiovascular risk after noncardiac surgery: preliminary data

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Background: Annually, 8 million patients suffer cardiovascular complications after noncardiac surgery and approximately 1 million die within 30-days. Early identification of at-risk patients may reduce perioperative morbidity and mortality. The revised cardiac risk index (RCRI) is a widely used tool for estimating risk of cardiovascular complications after noncardiac surgery, but it does not assess functional capacity. We present preliminary data on the utility of an objective measure of functional capacity, the six-minute walk test (6MWT), in addition to the RCRI in predicting the incidence of major cardiovascular complications 30-days after noncardiac surgery.

Methods: Following ethical approval, we initiated a prospective cohort study in two hospitals of the McGill University Health Centre (MUHC). Eligible patients were ≥50 years old with elective noncardiac surgery within 3 months, and ≥1 risk factors: hypertension, diabetes mellitus, dyslipidaemia, coronary artery disease, chronic kidney disease, transient ischemic attack (TIA), stroke, or peripheral vascular disease. Patients with significant physical or cardiopulmonary conditions preventing mobilization for 6 minutes were ineligible. The 6MWT was administered as per the American Thoracic Society guidelines during the preoperative clinic visit.

Separate binary logistic regressions examined the predictive utility of 6MWT distance (6MWD) in hundred-metre intervals on a composite score of death and myocardial infarction (MI), and individual cardiovascular complications at 30-days after surgery: death, MI, troponin elevation, congestive heart failure, atrial fibrillation, TIA, stroke, deep-vein thrombosis (DVT), pulmonary embolism, and major bleeding.

Results: Preliminary data are available for 480 out of a target 1,000 patients. Patients had a mean (SD) age of 68.15 (9.2) years, were predominantly male (58.2%), and 31% had cancer. Most patients had hypertension (80.7%) and dyslipidaemia (62.5%), with an RCRI score of 0-1 (83.7%). Orthopaedic (18.6%) or open intraperitoneal (14.1%) surgeries were most common.

The mean (SD) 6MWD was 397m (120m). The primary outcome of death or MI at 30-days postoperatively was observed in 6 patients (1.5%) and was not associated with 6MWD (OR=0.703 [95% CI = 0.079, 3.680], p = 0.487). For individual cardiovascular complications, 6MWD was only significantly associated with DVT (8 patients, 1.9%) 30-days after surgery (OR=0.499 [95% CI = 0.221, 0.864], p = 0.032).

Conclusion: In this preliminary analysis, the 6MWD was not associated with death or MI at 30-days, though we observed a low incidence of these events. A relationship between 6MWD and postoperative DVT may be emerging. With further data, we aim to more clearly define the risk predictive capabilities of the 6MWT alongside the RCRI.

Homozygous Familial Hypercholesterolemia (HoFH) in Canada

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Homozygous familial hypercholesterolemia (HoFH) is an orphan disease characterized by extremely high levels of plasma levels of LDL-C. Affected patients develop clinical atherosclerotic cardiovascular disease (ASCVD) in youth and survival > 30 years of age was unusual until the advent of medications and extracorporeal LDL filtration (apheresis) techniques. HoFH is an autosomal co-dominant condition defined as an LDL-C > 13 mmol/L in adults without treatment and homozygous or compound heterozygous mutations of the *LDLR* gene. HoFH has a genetic probability of ~1/250,000 and the rare diseases inventory Orphanet estimates its worldwide prevalence at 0.1/100,000 individuals. Canada is known to have several regions with a founder effect for HoFH and we identified 79 cases across the country. Data from other countries show a median survival of HoFH patients at < 40 years of age.

Clinical outcomes in HoFH patients, especially ASCVD events (fatal and non-fatal myocardial infarctions, strokes and peripheral vascular disease) and severe calcific aortic stenosis, are difficult to capture, in part because of the rarity of the disorder and the lack of registry focusing on this disease. The objective of our project is to obtain a comprehensive registry of HoFH in Canada, estimate the cost to society caused by HoFH burden of disease in Canada, and implement changes to advocate access to specialized care for these patients.

Here, we present preliminary data on our Canadian HoFH registry, including medical history, levels of LDL-C, treatments and outcomes of 21 HoFH patients.

We plan to use this data at provincial and national levels, in help with the Canadian Organization for Rare Diseases (CORD) and the Réseau Québecois des maladies orphelines (RQMO), to provide HoFH patients access to care, including PCSK9 inhibitors, orphan drugs such as lomitapide and evinacumab, and treatment techniques such as extracorporeal LDL filtration (apheresis). This work will provide important new health-related knowledge about the determinants of ASCVD risk and phenotypic manifestations of HoFH in Canada and examine the quality of life and burden to the healthcare system.

Impact of the Use of Z-Scores on the Intra-Subject Variability of CMR Mapping Between Different Field Strengths and Scanner Manufacturers

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Background: Cardiovascular Magnetic Resonance (CMR) T1 and T2 mapping is increasingly used for myocardial tissue characterization [1-3]. There is, however, substantial variability in measured values between vendors, scanners, field strengths, pulse sequences, and institutions. Recently, z-score distributions, indicating the deviation of samples from the population mean have been proposed to evaluate local normal values [4]. We hypothesized that the variability between scanners and field strengths is reduced in the same participant when evaluating z-scores instead of absolute values of normal native T1 and T2 mapping.

Methods: Twenty-nine healthy volunteers (*mean age* = 43 ± 16, 17 Male / 12 Female) underwent three CMR exams on three different scanners (1.5T Artist™, GE Medical Systems, USA; 3T Premier™, GE Medical Systems; and 3T Skyra™, Siemens Healthineers, Germany). For T1 mapping, we used a Modified Look Locker Inversion Recovery (MOLLI) 5-(3)-3 sequence on all three scanners. For T2 mapping, we used a True Fast Imaging with steady-state free precession (TRUFI) sequence on the 3T Skyra™, and a T2 Fast Spin Echo (FSE) sequence on both GE scanners. All images were obtained in basal and mid-ventricular short axis views of the left ventricle. All images were analyzed using cvi42 (Calgary, Canada). Global and segmental means were obtained for each slice and scaled to z-scores.

Results: The intra-class correlation (ICC) for global T1 and T2 mapping revealed a reduction in intra-subject variability when scaling to z-scores across all scanners. The ICC was greater for all twelve of the basal and mid-ventricular AHA heart segments for T1 mapping and the basal-anterior, -inferior, and -anterolateral wall for T2 mapping when normalizing to z-scores [5]. There was a moderately strong correlation for global T1 between the Artist and Premier (r=0.463*) and for T2 between the Artist and Skyra (r=0.612***). When comparing age-matched (*mean age*=~43) healthy subjects (*n1*=14, *n2*=15), significant differences in absolute global and segmental T1 and T2 values were observed between scanners (p<0.0001). However, repeated measures ANOVA reported no significant differences in z-scores of global T1 and T2 between scanners (p>0.05).

Conclusion: As expected, there were large amounts of intra-subject and inter-scanner variability in T1 and T2 mapping, which were significantly reduced in global and segmental T1 and global T2 when the data were expressed as z-scores. Therefore, the use of z-scores enables the comparability of mapping results between different MRI pulse sequences, field strengths, scanners, and vendors.

Risk of Hematopoietic Cancer in Congenital Heart Diseased Children with or without Genetic Syndromes

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Background: Individuals with genetic syndromes can manifest both congenital heart disease (CHD) and cancer due to possible common underlying pathways. However, reliable risk estimates of hematopoietic cancer (HC) among children with CHD based on large population-based data are scant. This study sought to estimate the risk of HC among children with CHD.

Method: We conducted a population-based analysis to estimate the cumulative incidence of HC in a cohort of children (0-18) born between 1999 and 2017, with at least one hospitalization records of CHD diagnosis. We merged the CIHI-Discharge Abstract Database, which regularly collects hospitalization and day surgery records in all Canadian provinces except Quebec, with the Quebec CHD database to develop the Canadian Congenital Heart Disease Database. Hematopoietic cancer and syndromes were both identified by hospitalization diagnoses. We used a modified Kaplan-Meier curve analysis to estimate the cumulative incidences (with 95% confidence intervals) up to 18 years of age, with death as a competing risk and stratified by the genetic syndrome status.

Result: We followed 143,881 CHD children from birth for 1,387,934 person-years. In this study population, 8.7% had genetic syndromes, and 911 HC cases were observed. The cumulative incidence of HC up to age 18 was 2.42% (95% CI: 2.10-2.73%) among children with a genetic syndrome and 0.83% (0.75-0.92%) without the syndrome. The incidence proportion was higher in the first six years of life than the subsequent 6-years intervals up to adulthood. Children with severe CHD lesions and genetic syndrome had a cumulative incidence of 2.95% (95% CI: 2.29-3.61%), whereas with non-severe CHD lesions and genetic syndrome had 2.23% (95% CI: 1.87-2.59%).

Conclusion: This is the first population-based analysis documenting that genetic syndromes in CHD children are a powerful predictor of hematopoietic cancers. The finding is essential in informing risk-stratified policy recommendations to protect CHD children from cancer.

Exposure to Low-Dose Ionizing Radiation from Cardiac Procedures and Risk of Malignancy in Children with Congenital Heart Disease

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Background: We have documented an association between cardiac low dose ionizing radiation (LDIR) exposure and cancer incidence among adults with congenital heart disease (CHD). Yet, there is limited data on the impact of cardiac LDIR in pediatric CHD (PCHD) who are more radiation sensitive. This study aimed to assess the association between cardiac LDIR exposure and cancer incidence in PCHD.

Methods: We performed a nested case-control study using the Quebec CHD database. The study population were children born between January 1st, 1988 and March 31st, 2010. They were followed from birth until age 18, death, time of first cancer diagnosis, or administrative censoring, whichever came first. Cancer cases were defined if having cancer hospitalization(s) or at least two outpatient cancer diagnoses made by selected specialists. Each cancer case was matched with 30 controls on age and sex at the time of first cancer diagnosis. LDIR exposure was measured as the cumulative number and dose of all types of LDIR procedures using a 6 months lag-time prior to the first cancer diagnosis for each case-control pair. Conditional logistic regression was performed for assessing the association between cancer incidence and cardiac LDIR exposure.

Results: A total of 418 cancer cases were matched with 12,540 controls. Cancer cases had a higher proportion of LDIR exposure (11.7% vs 6.7%) and a greater mean radiation dose (2.7 vs 1.4 mSv) though it did not reach statistical significance. The adjusted odds ratio (OR) for risk of cancer associated with cardiac LDIR exposure measured as a binary variable was 3.26 [95% confidence interval (CI): 2.07, 5.18]. When cardiac LDIR exposure was measured as a continuous variable, the adjusted OR for risk of cancer was 1.16 per 4 mSv increments of radiation dose (95%CI: 1.10, 1.21). Whether non-cardiac procedure exposure was measured as a binary or continuous variable, it was not associated with cancer incidence (OR=1.09, 95%CI: 0.80, 1.49) and (OR = 1.08, 95%CI: 0.79, 1.48), respectively.

Conclusion: We demonstrated an association between exposure to cardiac LDIR procedures and incident cancer risk in children with CHD. Studies are required to determine the threshold effect of LDIR exposure.

Psychosocial impacts of familial hypercholesterolemia: findings from systematic reviews of the literature

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Background: Familial hypercholesterolemia is a genetic disorder characterized by lifelong derangements in low-density lipoprotein cholesterol and premature atherosclerotic cardiovascular disease. The impacts of diagnosis and treatment on patients' psychosocial wellbeing has been poorly characterized. This is concerning given that nearly 1 in 300 people are estimated to be heterozygotes for this condition.

Objectives: We systematically reviewed the literature to identify studies examining relationships between familial hypercholesterolemia in its homozygous (HoFH) and heterozygous (HeFH) forms and anxiety, depression, and health-related quality of life (HRQL).

Methods: We conducted reviews in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) consensus guidelines. Quantitative and qualitative studies were eligible if they: (1) included patients with confirmed diagnoses of HeFH or HoFH and (2) examined associations with symptoms of anxiety, depression, or HRQL using validated tools. Qualitative studies were synthesized narratively. Where data permitted, we performed random-effects meta-analysis reporting standardized mean differences (SMD) with 95% confidence intervals (CI).

Results: Data from 5 studies including 113 participants showed that patients with HoFH experienced significant impairments in quality of life and high treatment burdens that compromised their educational attainment and employment. Few of these patients received psychological support in navigating their complex treatment challenges. Random-effects meta-analysis of 4 (n = 4,293) and 5 studies (n=5,098), respectively, showed that patients with HeFH had moderately lower symptoms of anxiety (SMD: -0.29; 95% CI -0.53, -0.04) and better mental HRQL (SMD: -0.10; 95% -0.20, -0.00) relative to general population controls. We found no significant differences in depressive symptoms (SMD: 0.04; 95% CI -0.12, 0.19) or physical HRQL scores (SMD: 0.02; 95% CI -0.09, 0.12). Importantly, we identified no published studies examining the incidence, severity or clinical course of anxiety or depressive disorders in HeFH or HoFH patients.

Conclusions: Our findings suggest that patients with HoFH may suffer significant disease-related impairments in quality of life. By contrast, patients with HeFH may benefit from lower anxiety symptoms and better HRQL relative to the general population. Future work should aim to elucidate relationships between these conditions and definitive mental health outcomes and evaluate interventions to improve quality of life.

Improving the Management of Obstetric Hypertensive Emergencies

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Background: Severe systolic or diastolic blood pressure (BP) elevations during pregnancy and postpartum are associated with increased risk of maternal stroke and adverse perinatal outcomes. Obstetric hypertensive emergency (OHE) is defined as persistent, severe hypertension, with 2 systolic BP > or = 160 mm Hg or diastolic BP > or = 110 mm Hg values taken 15-60 minutes apart. The objectives of this study were to identify care gaps in management of pregnant or postpartum patients with hypertensive disorders of pregnancy (HDP), and to define quality indicators for OHE management.

Methods: We retrospectively identified all pregnant and postpartum patients with a hospital discharge diagnosis of HDP from January 1 to December 31, 2019 at a tertiary care centre in Montreal, Canada. A retrospective cohort of patients with OHE was constructed. Data on baseline characteristics, OHE management, and individual patient outcomes were collected through chart review. OHE management was assessed according to 9 quality indicators (for inpatient management and discharge planning), pre-defined by a multidisciplinary panel of experts.

Results: Over the study period, 318 patients were diagnosed with HDP (gestational hypertension: 110, preeclampsia: 183, eclampsia: 2, chronic hypertension: 38). Of these, 22 (7%) had documented OHE. Median time from confirmed BP > or = 160/110 mm Hg to goal BP <155/105 mm Hg was 66 minutes (interquartile range 40-139 minutes). Goal BP was achieved within 60 minutes of confirmed severe BP in 11 (50%) patients. Antihypertensives were initiated within 30 minutes of confirmed severe BP in 11 (50%) patients, and appropriate antihypertensives were used in 11 (50%) patients. Process issues related to OHE management were identified in 15 (68%) patients, including failure to identify OHE (9, 41%), delayed treatment (5, 23%), and inappropriate treatment (13, 60%).

Conclusion: Care gaps in OHE management include lack of recognition of OHE, treatment delays and substandard treatment. These findings may be used by healthcare organizations to adopt and implement standardized treatment algorithms for OHE management.

P2X7 receptor knockout attenuates angiotensin II-induced hypertension, vascular injury and CD8+ T cell infiltration

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Background: The immune system plays an important role in the development of hypertension and cardiovascular injury; however, the driving force behind the initiation and maintenance of an immune response during hypertension has remained elusive. Elevated plasma adenosine triphosphate (ATP) levels have been observed in hypertensive patients, which could engage the immune system through activation of the purinergic receptor P2X7 (P2RX7). Pharmaceutical antagonism of P2RX7 reduced blood pressure (BP) in Dahl-salt sensitive rats fed a high-salt diet, while *P2rx7* gene knockout prevented deoxycorticosterone acetate salt-induced BP elevation and renal damage in mice. However, whether P2RX7 activation contributes to angiotensin (Ang) II-induced BP elevation and vascular damage through enhanced immune activation is currently unknown. We hypothesized that deletion of *P2rx7* would blunt Ang II-induced BP elevation, vascular injury and infiltration of activated immune T cells into perivascular adipose tissue (PVAT).

Methods: Ten-to-12-week-old male C57BL/6J male wild-type (WT) and *P2rx7–/–* mice were infused or not with Ang II (1000ng/kg/min) for 14 days. BP was determined by telemetry, mesenteric artery function and remodeling using pressurized myography, aortic stiffening by ultrasound and infiltration of activated immune T cells in PVAT by flow cytometry. IL-1β secretion from WT and *P2rx7–/–* bone marrow-derived macrophages (BMDM) and dendritic cells (BMDC) was assessed by ELISA.

Results: Lipopolysaccharide plus ATP stimulated IL-1β release from WT BMDMs (300±143 pg/mL) and BMDCs (749±36 pg/mL), but not from *P2rx7–/–* cells. Ang II-infused *P2rx7–/–* mice display a reduced systolic blood pressure (164±3 vs. 176±2 mm Hg, $P<0.05$) and pulse pressure (37±4 vs. 53±3 mm Hg, $P<0.001$) in comparison to WT mice. Ang II-infusion induced mesenteric artery endothelial dysfunction in WT mice (22% reduction in relaxation response to acetylcholine, $P<0.05$), which was absent in *P2rx7–/–* mice. Hypertrophic remodeling of the mesenteric arteries occurred in WT mice treated with Ang II (1.3-fold increase in media/lumen, $P<0.01$, and 1.3-fold increase in media cross-sectional area), whereas Ang II caused eutrophic remodeling in *P2rx7-/-* mice (1.2-fold increase in media/lumen only, $P<0.05$). Aortic stiffening occurred in WT mice treated with Ang II, demonstrated by an increased pulse wave velocity (7.7±0.7 vs. 5.9±0.3 m/s, $P<0.05$), accompanied by a 3.8-fold increased infiltration of activated CD8+ T cells in aortic PVAT ($P<0.001$), which were both absent in *P2rx7–/–* mice.

Conclusion: P2RX7 knockout attenuates Ang II-induced hypertension, vascular injury, and infiltration of activated CD8+ T cells into aortic PVAT.