Maurice McGregor
CARDIOVASCULAR
RESEARCH DAY

Thursday, May 11, 2023
8:25 a.m. - 3:35 p.m.

Scientific Planning Committee

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Judy Luu, MD PhD
Abhinav Sharma, MD PhD
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Our sincere thanks to our judges for their expertise in scoring all the abstracts submitted and a special thanks to Ms. Line Dufresne for her technical assistance.

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CME Accredited Event

RCPSC MOC Section 1
This program meets the accreditation criteria as defined by the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada and has been accredited by the Office for Continuing Professional Development, Faculty of Medicine and Health Sciences, McGill University for up to ***4 Section 1*** *(Accredited Group Learning Activity) credits/hours.*

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Acknowledgement of Institutional Sponsors

We acknowledge and greatly appreciate the support and involvement of our institutional sponsors as an integral part of the Maurice McGregor Cardiovascular Research Day.

McGill University Heath Centre – Research Institute
Faculty of Medicine
Department of Medicine

Program

Thursday, May 11, 2023

- *Oral Presentations as well as the Lucian Lecture will be held at the Institute of Community & Family Psychiatry (ICFP) which is located at **4333 Chem. de la Côte-Sainte-Catherine***
- *Poster Presentations, Awards and Closing Remarks will be held at the Carrefour Lea Polansky - K1 which is located at **3755 Chem. de la Côte-Sainte-Catherine***

8:00 - 8:25	Registration	Carrefour Lea Polansky - K1
8:25 - 8:30	Introduction	**Michael Goldfarb, MD, MSc**
8:25 - 8:30	Opening Remarks	**Ernesto L. Schiffrin, CM, MD, PhD, FRSC, FRCPC, FACP** Physician-in-Chief, Sir Mortimer B. Davis-Jewish General Hospital, Director, Hypertension and Vascular Research Unit, Lady Davis Institute for Medical Research, Distinguished James McGill Professor and Associate Chair, Department of Medicine, McGill University. Editor-in-Chief, The American Journal of Hypertension.
8:30 - 9:45	Oral Presentations Session #1 moderated by Judy Luu, MD, PhD	**8:30 -** Amir Razaghizad (clinical/pop.health) Sex-Specific Pathways in the Pathogenesis of Heart Failure in Diabetes: Insights from the EXAMINE Trial **8:45 -** Harry Moroz (clinical/pop.health) hART: Delivering Precision Medicine for patients with congenital heart disease with a heart-failure Attentive Risk Trajectory model **9:00 -** Karina Gasbarrino (basic science) Sex Differences in the Adipokine, Lipid, Immune, and Sex Hormone Profiles of Men and Women with Severe Carotid Atherosclerosis **9:15 -** Ahmed AlTurki (clinical/pop.health) A Meta-Analysis of Randomized Controlled Trials of Catheter Ablation for Atrial Fibrillation in Heart Failure with Reduced Ejection Fraction **9:30 -** Amanpreet Kaur (clinical/pop.health) Sex differences in the relationship between the age of diagnosis of hypertension and brain structure in midlife and older population: new insights from the UK Biobank **9:45 -** Ida Derish (basic science) Assessment of Hypertrophy and Mitochondrial Localization after Hypoxic Injury in Induced Pluripotent Stem Cell-Derived Cardiomyocytes
10:00 -10:30	Break	

10:30 - 12:00	Oral Presentations Session #2 moderated by Abhinav Sharma, MD, PhD	**10:30 -** Glisant Plasa (clinical/pop.health) Machine Learning and Oxygenation-Sensitive Cardiovascular Magnetic Resonance for Precise Patient Classification and Biomarker Identification in Cardiovascular Disease **10:45 -** Sam Amar (clinical/pop.health) Gestational age-specific markers associated with postnatal intervention in fetal suspicion of coarctation of the aorta **11:00 -** Jonathan Alejandro O'Connor Miranda (basic science) D-mannose supplementation decreases atherosclerotic lesions in ApoE-/- mice through regulation of gut microbiota composition and inflammation. **11:15 -** Paula Sanchez-Somonte (clinical/pop.health) Ultra-low-temperature cryoablation for ventricular tachycardia; a single centre experience **11:30 -** Justine Desrochers (clinical/pop.health) Inclusion of X chromosome variants modifies the strength of a coronary artery disease genetic risk score **11:45 -** Ding Yi Zhang (clinical/pop.health) High Coronary Calcium Burden Detected by Deep Learning Predicts Post-TAVR Mortality
12:00 - 1:00	**2022 Louis & Artur Lucian Award Lecture**	**Barbara Casadei, MD, DPhil, FRCP, FMedSci, FAHA, FESC** British Heart Foundation Professor of Cardiovascular Medicine Cardiovascular Theme Leader, NIHR Biomedical Research Centre Division of Cardiovascular Medicine BHF Centre of Research Excellence John Radcliffe Hospital University of Oxford **“Atrial fibrillation and cardioembolic stroke: A multidisciplinary look at an old problem”.**
1:00 - 1:30	Lunch	Carrefour Lea Polansky - K1
1:30 - 3:00	Poster Presentations	Poster viewing session and poster finalists
3:15 - 3:25	Break	
3:25 - 3:30	Awards	presented by Michael Goldfarb, MD, MSc
3:30 - 3:35	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

Barbara Casadei, MD, DPhil, FRCP, FMedSci, FAHA, FESC
British Heart Foundation Professor of Cardiovascular Medicine
Cardiovascular Theme Leader, NIHR Biomedical Research Centre
Division of Cardiovascular Medicine
BHF Centre of Research Excellence
John Radcliffe Hospital
University of Oxford

Dr. Casadei did her training in medicine and cardiology at the University of Pavia and Oxford. She subsequently completed her D.Phil. at the university of Oxford. She was appointed Senior Fellow of the British Heart Foundation and was promoted to Professor and British Heart Foundation Chair. In 2014, she became the lead of the Myocardial Biology Theme of the Oxford BHF Centre of Research Excellence and Deputy Head of the Division of Cardiovascular Medicine.

She is an international leader in her field. She is past-president of the European Society of Cardiology (ESC) and during her mandate she founded EuroHeart, an initiative supporting the assessment and improvement of quality of cardiovascular care in Europe, the cardiovascular Patient Forum, and the Women in the ESC. She is active in scientific advisory boards of prestigious institutions and research funding bodies nationally and internationally.

Dr. Casadei, who is the British Heart Foundation chair of Cardiovascular Medicine and honorary consultant cardiologist at the John Radcliffe, received the award for her seminal work on the molecular mechanisms underlying atrial fibrillation and heart failure. Her work has focused on the role of nitric oxide signaling in these pathologies. Her work has elucidated the role of a “neuronal isoform” of nitric oxide synthase (nNOS) in cardiomyocytes in the regulation of adrenergic responses, excitation-contraction coupling, atrial repolarization and myocardial remodeling after myocardial infarction. Importantly, over the years, Dr. Casadei has continued to advance the field and has identified tetrahydrobiopterin-regulated nNOS, as a cardioprotective mechanism in diabetic cardiomyopathy.

Abstracts for Oral Presentations (order of presentation)

Sex-Specific Pathways in the Pathogenesis of Heart Failure in Diabetes: Insights from the EXAMINE Trial

Amir Razaghizad[1], Joao Pedro Ferreira[2], Guang Zhang[1], William White[3], Cyrus R Mehta[4], George L Bakris[5], Faiez Zannad[6], Abhinav Sharma[1]

[1]McGill University, [2]University of Porto, [3]University of Connecticut, [4]Harvard University, [5]University of Chicago, [6]University of Nancy

Background:
Therapies reduce the risk of heart failure (HF) in type 2 diabetes (T2D), however, the excess risk of HF in patients with T2D and recent acute coronary syndromes (ACS) is greater in females versus males.

Methods:
To elucidate sex-differences in HF in T2D after ACS, we compared 92 circulating biomarkers (Olink® Cardiovascular II panel) in males and females for the outcome of heart failure hospitalization (HFH). We used data from the Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care (EXAMINE) trial. Sex-specific HF pathophysiology was interpreted with network and pathway over-representation analyses.

Results:
The EXAMINE trial enrolled 5,380 participants (32.1% females). Biomarker data was available in 95.4% of participants. Analyses revealed that 43 biomarkers were differentially expressed in HFH, of which 18 were sex-specific. Among these 43 biomarkers, interleukin-6 was identified as a central node for the pathogenesis of HFH in both males and females. Pathway over-representation analyses further revealed that biomarkers associated with inflammatory pathways related to endothelial-dysfunction and cardiac fibrosis, and mitogenic pathways associated with cardiac remodelling were more up-regulated in females than males developing HFH. Differential expression of 3 biomarkers (pentraxin-related protein 3, hydroxyacid oxidase 1, and carbonic anhydrase 5A) was independently associated with an increased risk of HFH in females but not in males (interaction $p > 0.05$).

Conclusion:
In patients with T2DM and ACS, interleukin-6 may play a central role in HF development among females and males. Females express higher levels of circulating proteins related to inflammatory and mitogenic pathways, reflecting sex-specific pathophysiology.

hART: Delivering Precision Medicine for patients with congenital heart disease with a heart-failure Attentive Risk Trajectory model

Harry Moroz[1], Yue Li[2], Ariane Marelli[1], Aihua Liu[1], Liming Guo[1]

[1]McGill Adult Unit for Congenital Heart Disease Excellence, [2]McGill University Department of Computer Science

Background:
Despite improvements in congenital heart disease (CHD) patient prognosis, lifelong comorbidities remain a concern. To address this, there has been a shift in management towards a proactive and lifespan-focused approach to care. This study uses large datasets to better comprehend the long-term disease progression of CHD patients, with the goal of providing precision medicine and personalized care through the use of deep learning.

Methods:
We developed hART, an attention-based deep-learning model to predict HF trajectories in CHD patients. Inspired by the transformer encoder, our model improves on previous limitations by modeling long and short-range dependencies while enhancing interpretability for clinicians. We evaluated hART on the Quebec CHD databases, which includes 137,493 patients, of whom 16,138 had at least one HF hospitalization. We utilized patient data, including diagnoses, hospitalizations, surgeries, comorbidities, and demographics. We evaluated the effectiveness of hART by examining differences in disease trajectory for different patient profiles, including those with genetic syndrome and severe CHD, as well as patients who died at different ages. Additionally, we computed individualized trajectories and extracted attention weights to identify how specific medical events contribute to rising predicted HF risk, providing personalized retrospective risk trajectory for each patient.

Results:
Our model surpassed all baseline and existing models, achieving an AUPRC score of 0.282 and an AUROC score of 0.967 with 80% accuracy in predicting heart failure occurrence within 6 months. Our analysis revealed that patients with severe CHD have a higher lifelong risk of heart failure, with a significant increase in HF events after age 50. Patients with genetic syndromes have a higher risk of HF until age 40, then their risk trajectory is similar to those without genetic syndromes. Our hART model also compared the HF risk trajectories of patients with CHD who died at different ages, showing that younger age of death correlates with an earlier significant increase in HF risk. Furthermore, we presented three case studies illustrating the impact of specific medical events and timing on the HF trajectory.

Conclusion:
Our study offers a valuable framework for examining the evolving risk of thousands of CHD patients, facilitating personalized care and informed decision-making. Our findings highlight the potential of hART to aid in risk stratification, intervention timing optimization, and deeper disease understanding for patients with CHD. Finally, hART's success in modeling disease trajectories highlights its potential for predicting other medical conditions and guiding the management of chronic diseases and comorbidities.

Sex Differences in the Adipokine, Lipid, Immune, and Sex Hormone Profiles of Men and Women with Severe Carotid Atherosclerosis

Karina Gasbarrino[1], Huaien Zheng[1], Edward Daly[2], Stella S. Daskalopoulou[1]

[1]Division of Experimental Medicine, Department of Medicine, Faculty of Medicine, Research Institute of McGill University Health Centre, McGill University, Montreal, Quebec, Canada, [2]Clinical Proteomics and Mass Spectrometry, Research Institute of McGill University Health Centre, Montreal, Canada

Background:
Circulating markers that reflect sex-specific features in the plaque should be explored for better prediction of stroke risk in women and in men. Herein we investigated 1) sex differences in the adipokine, lipid, and immune circulating profiles of men and women with stable versus unstable plaques, and 2) sex-specific differences in circulating sex hormone levels.

Methods:
Pre-operative plasma and sera samples were collected from men and women undergoing a carotid endarterectomy (n=460), to perform adipokine, lipid, immune and sex hormone profiling. Specifically, sex hormones were analyzed via in-house liquid chromatography-tandem mass spectrometry methods. Plaque composition and stability were determined by gold-standard histological classifications.

Results:
Men had more unstable plaques than women ($P<0.001$), exhibiting greater plaque hemorrhage, a larger lipid core, and a greater number of inflammatory cells ($P<0.001$). Men also had a greater proportion of circulating monocytes than women ($P=0.006$), while women had higher HDL-C, apoA-I, and total and high molecular-weight (HMW) adiponectin levels ($P<0.001$), irrespective of plaque instability. Specifically in men, low total WBC counts, a high monocyte to WBC ratio, a low basophil to WBC ratio, and high LDL-C levels were independently associated with greater plaque instability, while similar associations were observed in women with an increase in the basophil to WBC ratio and a decrease in the HMW to total adiponectin ratio. Higher circulating testosterone and lower 17ß-estradiol [E_2] levels, as well as a higher testosterone to E_2 ratio reflected plaque instability and unstable plaque composition in men. While no consistent relationship was observed in women between sex hormone levels and plaque instability, a higher testosterone to E_2 ratio was associated with less fibrosis and greater cap inflammation.

Conclusion:
Our study demonstrated sex-specific differences between older men and postmenopausal women with severe carotid atherosclerosis, not only at the level of the plaque but also at the level of the circulation, with women displaying more favourable adipokine, lipid, and immune profiles compared to men. Furthermore, we are the first to reveal several adipokine, lipid, and immune parameters to serve as independent sex-specific markers of plaque instability. Finally, we identified circulating sex hormone levels to be associated with sex-specific differences observed at the level of the circulation and the plaque. Pending validation, these markers could be used as predictive clinical markers of plaque instability in men and women.

A Meta-Analysis of Randomized Controlled Trials of Catheter Ablation for Atrial Fibrillation in Heart Failure with Reduced Ejection Fraction

Ahmed AlTurki[1], Ahmed Dawas[1], Thao Huynh[1], Vidal Esssebag[1]

[1]McGill University Health Center

Background:
Catheter ablation of atrial fibrillation (AF) in patients with heart failure with reduced ejection fraction (HFrEF) improved symptoms and left ventricular ejection fraction (LVEF) and reduced all-cause mortality in one large trial. We aimed to evaluate the hypothesis that AF catheter ablation is superior to medical therapy in patients with AF and HFrEF with regards to mortality and heart failure hospitalizations.

Methods:
We searched electronic databases for all RCTs that compared AF catheter ablation and medical therapy including anti-arrhythmic drug therapy. We used random-effects models were used to summarize the studies. The primary outcome was all-cause mortality. The secondary outcome was heart-failure hospitalizations (HHF). We completed a subgroup analysis of trials with at least two years of follow-up.

Results:
We retrieved and summarized ten randomized controlled trials, enrolling 2,240 patients (1,121 in the catheter ablation arm and 1,119 in the medical therapy arm). The baseline characteristics were similar in both arms. Compared with medical therapy (including use of anti-arrhythmic drugs, AF catheter ablation was associated with a reduction in mortality (risk ratio 0.63; 95% confidence interval [CI]: 0.49 to 0.81; P<0.0001) and HHF (risk ratio 0.66; 95% CI: 0.51 to 0.85; P = 0.0001). Similar results were obtained when only trials with at least two years of follow-up were included. AF catheter ablation was associated with a reduction in mortality compared to medical therapy (risk ratio 0.61; 95% confidence interval [CI]: 0.44 to 0.84; P=0.0002) and HHF (risk ratio 0.60; 95% CI: 0.49 to 0.74; P < 0.0001)

Conclusion:
Catheter ablation for AF significantly reduced mortality and HHF in patients with HFrEF compared to medical therapy even with the use of AAD. These results were consistent even when restricted to trials with longer-term outcomes. Catheter ablation of AF should be considered in patients with AF and HFrEF.

Sex differences in the relationship between the age of diagnosis of hypertension and brain structure in midlife and older population: new insights from the UK Biobank

Amanpreet Kaur[1], Chelsea Pozzebon[1], Hassan Behlouli[2], M. Natasha Rajah[3], Louise Pilote[2]

[1]McGill University, [2]Research Institute of McGill University Health Centre, [3]Department of Psychiatry, McGill University

Background:
Hypertension is an established leading risk factor for morbidity and mortality from vascular diseases across the lifespan. Early adulthood to midlife high blood pressure has been linked to later reduced brain volume and white matter hyperintensities, both of which are hallmarks of cerebral small vessel disease (CSVD). Independent of blood pressure control, the age of hypertension diagnosis has been identified as a unique contributor to brain structural changes related to cerebral small vessel disease. However, whether the association of age at diagnosis of hypertension with CSVD-related brain atrophy differs between females and males is not fully understood. Therefore, our objective was to assess for sex differences in the association between the age at diagnosis of hypertension and CSVD-related brain structural changes (lower total brain volume and higher volume of white matter hyperintensities).

Method:
We used data from the UK Biobank, a prospective cohort study of over 500,000 participants aged 40 to 69 years enrolled between 2006 and 2010. We selected participants with a known age of diagnosis of hypertension who had also obtained a brain MRI between 2014 and 2019 (n = 9,410) and stratified by age of diagnosis of hypertension (<35 years, 35-44 years, 45-54 years, 55-64 years, ≥65 years old) and sex. Using propensity score matching a control participant with MRI data but no hypertension was chosen at random. Generalized linear models were used to determine changes in brain structure as a function of age of hypertension diagnosis and sex while controlling for vascular risk factors and demographic covariates.

Results:
For the total brain volume (adjusted for head size), there was a trend for lower brain volume males in younger age group of hypertension diagnosis (<35 years) of diagnosis (β (95%CI, −23088.6 [−42244.3 to −3932.9]mm^3, p=0.02), 35 to 44 years (−7003.7 [−15516.5 to 1509]mm^3), and 45 to 54 years (−5260.5 [−9882.6 to −638.4]mm^3) but not in females. The volume of white matter hyperintensities was greater in both males (β (95%CI, 1488.1 [1149.2 to 1827]mm^3) and females (1700.1 [1351.9 to 2048.3]mm^3) than in those without hypertension.

Conclusion:
Hypertension diagnosed in mid-life was associated with smaller brain volumes in males. However, both males and females with hypertension had a higher volume of white matter hyperintensities, despite not being associated with younger age of diagnosis of hypertension. Therefore, sex-specific analyses are necessary to uncover effect of hypertension related to CSVD in males and females.

Assessment of Hypertrophy and Mitochondrial Localization after Hypoxic Injury in Induced Pluripotent Stem Cell-Derived Cardiomyocytes

Ida Derish[1], Elise Rody[2], Ludovic Mouttet[1], Renzo Cecere[1, 2]

[1]Department of Experimental Surgery, [2]Division of Cardiac Surgery

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 restricted oxygen leads to hypoxia-mediated cardiac damage, triggering apoptotic pathways within cardiomyocytes. Critically, cardiac tissue cannot regenerate, leaving survivors with a permanently damaged myocardium, a reduced quality of life, and disproportionate cardiac-related mortality. Unfortunately, cardiovascular patient-specific differences with regards to hypoxic injury remain poorly understood. Recently, induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) have gained traction to model heart disease *in vitro*. Previously, our group showed that iPSC-CMs derived from dilated cardiomyopathy (DCM) patients exhibited altered contractility, viability, metabolic activity, and calcium handling when compared to healthy controls. We hypothesized that DCM patient-derived iPSC-CMs will exhibit a more profound disease phenotype in response to hypoxic injury than iPSC-CMs derived from healthy donors. To gain additional insight, we analyzed hypertrophic response and mitochondrial localization within iPSC-CMs after hypoxia. With a more in-depth iPSC-CM characterization, we demonstrated that hypoxia-injured iPSC-CMs recapitulate a diseased phenotype and can be used to explore various mechanisms of the disease.

Methods:
First, we generated iPSCs (n=3 healthy donors, n=5 cardiomyopathic patients). from peripheral blood through transfection of reprogramming factors (Oct4, Sox2, Lin28, Klf4, L-Myc) and performed an assessment of cell line quality via immunocytochemistry, RT-PCR and trilineage differentiation. After iPSC-CM differentiation, we confirmed the expression of prominent cardiac markers via immunocytochemistry. We optimized our hypoxic conditions by subjecting iPSC-CM lines to 0%, 0.4% or 1% oxygen (for 6, 12 or 24 hours) mimicking hypoxic injury, and performed Crystal Violet and AlamarBlue to assess viability and metabolic activity of the cells. Finally, we stained the iPSC-CMs with MitoTracker, ActinGreen and NucBlue, imaged the cells on the confocal microscope and performed analysis on the ZEN software.

Results:
DCM patient-derived iPSC-CMs had significantly decreased viability and metabolic activity when compared to the controls, under normoxic ($p<0.01$) and hypoxic conditions ($p<0.001$). We also found preliminary differences in cell area ($p<0.01$) and mitochondrial localization ($p<0.05$). Further insight is required into pathways that might cause these functional outcomes.

Conclusion:
These results suggest that the detected differences at the cellular level after hypoxia-induced injury might be translatable to the inter-individual variability currently observed in the patient population. With this preliminary study, we hope to shift the focus towards these patient-specific differences *in vitro*, in the search for tailored therapies and a higher standard of care for CVD patients.

Machine Learning and Oxygenation-Sensitive Cardiovascular Magnetic Resonance for Precise Patient Classification and Biomarker Identification in Cardiovascular Disease

Glisant Plasa[1], Elizabeth Hillier[1], Judy Luu[1], Mitchel Benovoy[2], Matthias Friedrich[1]

[1]McGill University Health Center, [2]Area 19 Medical

Background:
Oxygenation-Sensitive Cardiovascular Magnetic Resonance (OS-CMR) is a novel non-invasive technique that uses myocardial oxygenation to investigate vascular function. This technique has demonstrated outstanding potential for diagnosing and classifying patients presenting with various cardiac conditions. However, the large number of biomarkers available from scans complicates the data analysis. Using OS-CMR data, this study aimed to develop and evaluate a machine learning (ML)-based model for biomarker selection and disease classification to facilitate data analysis for researchers and clinicians in this emerging field.

Methods:
The data used for the ML-based model was derived from two short axis slices of OS-CMR studies performed on a 3T MRI system. The ML model was initially developed and tested on a data set of 28 patients with suspected coronary artery stenosis (CAD) and 24 healthy volunteers. The model was further validated in a study of 31 adult patients born preterm (less than 27 weeks) and 32 healthy volunteers. Mutual information criteria (MIC) and ANOVA feature selection methods were used to identify relevant and essential features in each dataset. A classifier trained on the well-selected features is subsequently used to compare the disease state classification performance of the selected markers to a null set of features (random features). We report the mean Area Under the Receiver Operating Characteristic Curve (AUROC) as performance accuracy.

Results:
When using selected markers, our model could classify patients with 94% (+/- 6%) and 82% (+/- 9%) accuracies for datasets 1 and 2, respectively. In comparison, models trained on the null features had 67% (*+/-10%*) and 55% (*+/-11%*) classification accuracies for datasets 1 and 2, respectively. Hence, we report significantly improved performance of disease classification ($p<0.05$) in both studies when using our feature selection technique.

Conclusion:
Our feature selection and biomarker validation pipeline showed improved accuracy for patient classification in both investigated cardiac conditions. The selected biomarkers are intended to assist clinicians and researchers in locating precise segments or cardiac phases where disease states become most apparent. Our model can pinpoint areas of interest so that clinicians can focus on the relevant heart regions and gain a more comprehensive understanding of how a particular cardiac condition may manifest in patients. The potential to significantly streamline this process will allow OS-CMR to be efficiently applied in routine clinical settings.

Gestational age-specific markers associated with postnatal intervention in fetal suspicion of coarctation of the aorta

Sam Amar[1], Shiran Sara Moore[2], Punnanee Wutthigate[3], Amanda Ohayon[4], Daniela Villegas Martinez[1], Jessica Simoneau[1], Claudia Renaud[5], Gabriel Altit[1]

[1]Division of Neonatology, Department of Pediatrics, McGill University Health Centre - Montreal Children's Hospital, Montreal, Quebec, Canada, [2]Division of Neonatology, Dana Dwek Children's Hospital, Tel Aviv Medical Centre, Tel Aviv, Israel, [3]Division of Neonatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [4]Department of Experimental Medicine, Department of Pediatrics, McGill University, Montreal, Quebec, Canada., [5]Division of Pediatric Cardiology, Department of Pediatrics, McGill University Health Centre - Montreal Children's Hospital; Montreal, Quebec, Canada

Background:
Fetal diagnosis of coarctation of the aorta (CoA) is currently associated with a high false-positive rate. Most predictive markers may be gestational age (GA)-specific. We sought to establish a set of gestational age-specific traditional and speckle-tracking fetal echocardiography (STE) markers predictive of true CoA in neonates with a prenatal suspicion.

Method:
Retrospective case-control study. We compared the fetal ventricular and arch dimensions, as well as the deformation parameters by STE, of infants who required a postnatal intervention for their CoA to those who did not. Cohort was stratified based on gestational age before or after 30 weeks. Data extractors were masked to the outcome. The first fetal echocardiogram available was used.

Results:
75 newborns with a fetal echocardiography performed between October 2013 and May 2022 for an antenatal suspicion of CoA were included, of which 59 (79%) had an aortic arch with non-significant obstruction upon ductal closure, and 16 (21%) underwent a neonatal intervention for a confirmed CoA. Before 30 weeks GA, the right ventricular to left ventricular (RV/LV) end-diastolic width and end-diastolic area (EDA) ratios were most associated with postnatal CoA confirmation (AUCs of 0.96 and 0.92). After 30 weeks GA, the RV/LV end-diastolic width ratio (AUC=0.95), the Z-score for the ascending aorta (AUC=0.93), and the LV end-diastolic width Z-score (AUC=0.91) performed best. A decreased RV peak longitudinal strain was observed in those who developed true CoA, and performed well by ROC analysis after 30 weeks (AUC=0.85). In the overall cohort, the RV/LV EDA ratio was the most sensitive predictor of CoA and identified all cases with CoA. Indeed, a cut-off >1.24 had a specificity of 69.5% and a sensitivity of 100% (receiver operating characteristic curve with an area under the curve of 0.88).

Conclusion:
We outlined sensitive and specific fetal markers associated with postnatal CoA based on gestational age at suspicion. These markers can be used to refine prenatal diagnostic accuracy, which could allow for a better triaging of fetuses based on their risk of developing CoA postnatally.

D-mannose supplementation decreases atherosclerotic lesions in ApoE-/- mice through regulation of gut microbiota composition and inflammation.

Jonathan Alejandro O'Connor Miranda[1, 2, 3], Talin Ebrahimian[1, 2, 3], France Dierick[1, 2, 3], Jaclyn Itzcovitch[1, 2, 3], Maria Kotsiopriftis[1], Stephanie Lehoux[1, 2, 3]

[1]Lady Davis Institute, [2]McGill, [3]Jewish General Hospital

Background:
D-mannose, a C−2 epimer of glucose, is an important monosaccharide for protein glycosylation that is widely distributed in body fluids and tissues. Interestingly, D-mannose supplementation has been shown to alter gut microbiota and to prevent obesity in young mice fed a high fat diet (HFD). Furthermore, both in vitro and in vivo studies have shown that mannose exhibits potent anti-inflammatory properties. We hypothesized that D-mannose supplementation would alleviate the pro-atherogenic effects of HFD by regulating the gut microbiota and inflammation.

Methods & results:
ApoE$^{-/-}$ mice were fed a high fat diet (HFD) for 9 weeks. Concurrently, they had access to tap water containing 0, 5, or 20% D-mannose. No differences in body weight, lipid levels, or glucose tolerance were observed among the groups. We found that atherosclerotic plaque burden (mm^2), determined by Oil red O staining, was significantly ($P<0.01$) reduced in mice receiving 5 and 20% mannose compared with 0% controls, both in the aortic sinus (0.23±0.03 (5%), 0.23±0.05 (20%) vs 0.39±0.04 (0%)) and the brachiocephalic artery (0.046±0.007 (5%), 0.031±0.005 (20%) vs 0.080±0.006 (0%)). Furthermore, plaques of 20% mannose mice displayed a significant 40% increase in a-smooth muscle actin content compared with 0% mouse lesions, suggesting that mannose stabilizes atherosclerotic plaques. Flow cytometry of blood revealed a reduction of pro-inflammatory Ly6C^{HI} monocyte subtypes by 25% in 5 and 20% mannose-treated mice vs 0% ($P<0.01$). Likewise, circulating neutrophils, whose numbers nearly tripled following HFD, remained at levels observed in chow-fed mice in the mannose groups. HFD and mannose feeding also altered the intestinal microbiome. Gut microbiota 16S sequencing analysis indicated a significant increase in Firmicutes/Bacteroidetes ratio by 2.7-fold in mice fed a HFD (6.1±1.5) compared with chow (2.0±0.3). Interestingly, this increase was prevented by 20% mannose supplementation (2.5±0.1). In addition, 5 and 20% mannose treatment reduced the proportion of TLR4-expressing F4/80+ macrophages among cells of the intestinal lamina propria in HFD mice (4.3±0.6% (0%) vs 2±0.4 (5%) and 1±03 (20%), $P<0.01$). Concurrently, plasma LPS levels increased by 2-fold in HFD-fed mice (12±2.1EU/ml) compared with chow controls (6±0.4EU/ml) and 20% mannose prevented this increase (8.7±1.5EU/ml). However, no difference in tight junctions for gut permeability was observed.

Conclusion:
Our results show in ApoE$^{-/-}$ mice fed a HFD, oral mannose supplementation reduces atherosclerotic lesions and increases plaque stability. These protective effects of mannose could possibly occur through a regulation of gut microbiota composition and LPS-induced intestinal inflammation, which influence monocytosis and neutrophilia.

Ultra-low-temperature cryoablation for ventricular tachycardia; a single centre experience

Paula Sanchez-Somonte[1], Luiz Gustavo Bravosi Da Rosa[1], Valeria Angleso[1], Vladimir Poletaev[1], Ahmed Alturki[1], Martin Bernier[1], Jacqueline Joza[1], Atul Verma[1], Vidal Essebag[1]

[1]MUHC

Background:
Endocardial catheter ablation for ventricular tachycardia (VT) may fail owing to the inability to deliver transmural lesions. In order to create fully transmural lesions, ultra-low-temperature cryoablation (ULTC) has been developed which uses near-critical nitrogen and is able to generate temperatures as low as −196°C. We report a series of 17 cases that underwent ULTC at MUHC, representing the largest single center experience reported until the data..

Methods:
17 patients with ischemic and nonischemic cardiomyopathy, with monomorphic drug-refractory VT who had failed at least one antiarrhythmic underwent VT ablation with ULTC at our institution. After a voltage map, the mapping catheter was replaced with the ULTC catheter. ULTC lesions were applied over a fixed duration of time (60-180 s), followed by at least a 60-second thaw and another application at the original duration (freeze-thaw-freeze). Duration of time was selected depending on the wall thickness of the left ventricle (LV) monitored with intracardiac echo (ICE) to achieve tissue depths of 4.5-7.5 mm .

Results:
Baseline left ventricular ejection fraction was 31.8 ± 8.1%, mean age was 69.9 ± 11.3 years; 94% were male. A total of 24 VTs were induced prio ablation (1.5 VT per patient). Mean procedure time was 2.6±0.8 hours, mean ablation time 23.3 ±8.5 minutes and mean fluoroscopy time 25.6±8.8 minutes. A total of 156 cryablation lesions were delivered (9.2±4.2 lesions per patient). Of the 24 VTs induced, all of them remained non-inducible at the end of the procedure. Complications included 1 pericardial effusion that required drainage. From 17 patients, 15 (88%) were discharged within the first 24 hours post ablation.

Conclusion:
ULTC is feasible and permits control of monomorphic VT during VT ablation procedure in drug-refractory patients.

Inclusion of X chromosome variants modifies the strength of a coronary artery disease genetic risk score

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Background:
Coronary Artery Disease (CAD) is the leading cause of death worldwide and incurs a high societal burden. Genome wide association studies (GWAS) have identified many variants that contribute to CAD, although many have small effects. However, when these variants are combined into a genetic risk score (GRS), their sum demonstrates a stronger effect. Previous GWAS and GRS efforts have failed to adequately assess the impact of X chromosome (X-chr) variants.

Methods:
Recently nine X-chr SNPs were discovered in a Million Veteran Program (MVP) GWAS of CAD including myocardial infarction (MI). We examined these SNPs as a X chromosome CAD GRS in men and women separately as well as together in 344,130 unrelated individuals of European ancestry from the UK Biobank (UKB) with 23,752 incident CAD events in generalized linear models. We also performed a sex stratified GWAS of chromosome X in UKB with 199,006 men and 233,674 women of European ancestry, respectively.

Results:
We tested the nine X-chr SNPs that were significant in the MVP in the men and women of UKB together and separately. With men and women combined, we observed an association between the X-chr GRS with CAD, including age and sex (Odds ratio (OR) per standard deviation (SD) (95% Confidence Interval (CI)), 1.08 (1.05,1.12); $P = 4.52\times10^{-06}$). When we performed the analysis separately, the X-chr GRS had a stronger effect in men than in women (OR (95% CI), 1.11 (1.06, 1.17), $P = 3.77\times10^{-05}$ for men; OR (95% CI), 1.06 (1.01, 1.11), P = 0.02 for women). In the sex-stratified UKB GWAS, six SNPs out of nine from MVP were significant in men ($p < 0.05$) whereas only two SNPs out of those six SNPs significant in men were significant in women ($p < 0.05$).

Conclusion:
Stronger effects of X-chr SNPs in men than in women in the UK Biobank highlights the potential contribution of these SNPs to sex-specific mechanisms in CAD etiology.

High Coronary Calcium Burden Detected by Deep Learning Predicts Post-TAVR Mortality

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Background:
The emergence of transcatheter aortic valve replacement (TAVR) provides patients with aortic stenosis (AS) with a minimally invasive procedural option to replace their aortic valve, and consequently, reduce mortality and symptoms of valvular dysfunction. Coronary artery disease (CAD) can potentially modulate outcomes of TAVR, although the association is more complex than causal. In the current management paradigm, asymptomatic CAD lesions do not routinely receive coronary intervention pre-TAVR.

Hypothesis:
We aim to determine whether a high quantitative burden of cardiovascular calcification would be predictive of short-term post-procedural outcomes in TAVR patients.

Methods:
Our team conducted a post-hoc analysis on patients enrolled in the multicenter FRAILTY-AVR cohort study. We leveraged our 3-Dimensional U-Net deep learning pipeline to detect and quantify coronary artery calcification (CAC), aortic valve calcification (AVC), mitral annular calcification (MAC), and thoracic aorta calcification (TAC) from pre-procedural CT images. CAC score was computed by the Agatston method, and AVC, MAC, and TAC were quantified by volume. The primary outcome was all-cause mortality at 30 days, adjusted for revascularization, surgical vs. transcatheter approach, and cardiovascular comorbidities.

Results:
The study sample consisted of 319 patients with a median age of 83 and EuroSCORE II of 0.066, among which 40% are female. The adjusted odds ratio for 30-day mortality were 1.14 (1.02-1.26, p=0.017) per 100 unit increment of the CAC score, 0.99 (0.98-1.01, p=0.45) per 100 mm^3 volume increment of TAC, 0.95 (0.84-1.07, p=0.40) per 100 mm^3 volume increment of AVC, and 1.00 (0.95-1.06, p=0.96) per 100 mm^3 volume increment of MAC. The median CAC score was 551 (IQR 72, 551).

Conclusion:
High coronary artery calcium burden quantified by our machine learning pipeline was associated with short-term post-procedural mortality. This raises the opportunity to improve our stratification of asymptomatic CAD to inform management.

Abstracts for Poster Presentations (alphabetical order)

58- Prediction of 1-Year Mortality in Cardiovascular Patients Using A Novel Bioimpedance-Based Machine Learning Pipeline

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Background: Bioelectrical Impedance Analysis (BIA) is a non-invasive test to assess body composition and physical frailty. The prognostic value of BIA is less certain in acute cardiovascular patients, because fluid shifts and illness-related variations may theoretically affect the results. We hypothesized that machine learning techniques could be used to generate more accurate results that are applied in this patient population.

Methods: Our prospective multicenter study collected BIA data from 346 patients hospitalized with acute cardiovascular disease using the InBody S10 device. We assessed all-cause survival at 1-year through telephone interviews and electronic medical records. This survival data was the output and the raw BIA data features were the inputs entered into our autoML platform that iteratively tested different combinations of models, hyperparameters, variables, and variable transformations.

Results: Our results showed that multiparametric BIA data, combined with an ensemble network of LightGBM and XGBoost machine learning models, was able to predict 1-year mortality with high accuracy (AUC 0.826). The optimal model leveraged 116 features, of which 50 KHz trunk reactance had the highest feature importance. None of these features required manual data collection, and the incremental value of adding such features is under study.

Conclusion: Our findings suggest that BIA can be used as a non-invasive tool to rapidly predict prognosis after an acute cardiovascular hospitalization. Further research is needed to validate our findings in larger and more diverse populations.

46 - Comparative analysis of common dense Optical Flow methods for pixel tracking across CMR short-axis sequences

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Background:
Cardiac magnetic resonance (CMR) is a non-invasive imaging technique used to assess the structure and function of the heart. Myocardial strain, a measure of heart muscle deformation during the cardiac cycle, can be extracted from CMR short-axis cine images. Dense optical flow is a computer vision technique used to estimate pixel motion in image sequences, which can be used in CMR to track myocardium pixels throughout the cardiac cycle and compute myocardial strain.

This study aimed to identify the optimal dense optical flow method for tracking myocardium pixels.

Method:
Thirteen deep optical flow methods from two popular open-source software libraries were tested: 1) the Open Source Computer Vision Library: Farneback Optical Flow, SimpleFlow, DeepFlow, PCA Flow, and Sparse to Dense Flow (SDF) ; and 2) OpenMMLab: FlowNet, FlowNet2, Iterative Residual Refinement (IRR), LiteFlowNet, LiteFlowNet2, MaskFlowNet, PWC-Net, and Recurrent All Pairs Field Transforms (RAFT).

These methods were tested on a cine series of CMRI short-axis images (3T MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) in 5 patients (4 Male, 1 Female, average age 31.6, coronary artery disease). Each frame had a corresponding binary colored myocardium segmentation mask created using human corrected convolution neural networks.

Each method was utilized to generate a flow vector matrix for consecutive pairs of frames within each sequence (such as frame 1 and frame 2, frame 2 and frame 3, and so on) during the evaluation process. The matrix was then applied to the mask of the first frame inside the pair to generate the mask of the second frame. Generated mask and original mask were then compared using the Dice Index (DI) and the Hamming Distance (HD). Averages were taken and compared between methods.

Results:
First value represents HD, second value represent DI. The methods in OpenCV: DeepFlow (39.05, 0.902), Farneback (46.44, 0.877), SimpleFlow (49.4, 0.884), PCA (51.6, 0.852), SDF (59.1, 0.815). The methods in OpenMMLab: FlowNet (57.0, 0.836), FlowNet2 (68.5, 0.771), IRR (52.9, 0.855), LiteFlowNet (68.7, 0.782), LiteFlowNet2 (60.8, 0.821), MaskFlowNet (52.0, 0.864), PWC-Net (51.9, 0.866), RAFT (49.0, 0.878).

Conclusion:
In general, a Dice Index of 0.7 or above is considered to be good for medical image segmentation tasks. The results imply that the DeepFlow algorithm is the best method for measuring myocardial strain using dense optical flow.

3 - ACE2 is involved in SARS-CoV-2 induced endothelial cell inflammation independent of viral replication.

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Background:
COVID-19 association with cardiovascular disease is thought to be due to endothelial cell inflammation. ACE2 interactions with SARS-CoV-2 spike protein S1 subunit is important to viral infection. Here we questioned whether SARS-CoV-2 induces vascular inflammation via ACE2 and whether this is related to viral infection.

Methods:
Human microvascular endothelial cells (EC) were exposed to recombinant S1p (rS1p) 0.66 µg/mL for 10 min, 5h and 24h. Gene expression was assessed by RT-PCR and levels of IL6 and MCP1, as well as ACE2 activity, were assessed by ELISA. Expression of ICAM1 and PAI1 was assessed by immunoblotting. ACE2 activity was blocked by MLN4760 (ACE2 inhibitor) and siRNA. Viral infection was assessed by exposing Vero E6 (kidney epithelial cells; pos ctl) and EC to 10^5 pfu of SARS-CoV-2 where virus titre was measured by plaque assay.

Results:
rS1p increased IL6 mRNA (14.2±2.1 *vs.* C:0.61±0.03 2^-ddCT) and levels (1221.2±18.3 *vs.* C:22.77±3.2 pg/mL); MCP1 mRNA (5.55±0.62 *vs.* C:0.65±0.04 2^-ddCT) and levels (1110±13.33 *vs.* C:876.9±33.4 pg/mL); ICAM1 (17.7±3.1 *vs.* C:3.9±0.4 AU) and PAI1 (5.6±0.7 *vs.* C: 2.9±0.2), $p<0.05$. MLN4760, but not rS1p, decreased ACE2 activity (367.4±18 *vs.* C: 1011±268 RFU, $p<0.05$) and blocked rS1p effects on ICAM1 and PAI1. ACE2 siRNA blocked rS1p-induced IL6 release, ICAM1, and PAI1 responses as well as rS1p-induced NFκB activation. EC were not susceptible to SARS-CoV-2 infection, while the virus replicated well in Vero E6.

Conclusion:
rS1p induces an inflammatory response through ACE2 in endothelial cells; an effect that was independent of viral infection.

6 - Perception of cardiovascular risk in familial hypercholesterolemia according to sex

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Background:
Familial hypercholesterolemia (FH), a common inherited genetic condition, is characterized by elevated LDL-C and premature cardiovascular disease (CVD). Recent data indicate an under-treatment of women with FH, which could be attributed to women having a different perspective of FH compared with men.

Objective:
To characterize the role of sex in the perception of the ASCVD risk associated with FH.

Methods:
A survey investigating the role of sex in the perception of FH was created and sent to 1073 FH patients at the MUHC and UBC lipid clinics, using a prospective cohort study design.

Results:
A total of 412 patients (51.9% men) participated in the survey; mean age was 56.2±14.4y. There was a higher proportion of men with ASCVD than women (41.5% vs. 16.5%, respectively, $p<0.001$). Analyses of the survey responses showed a statistically significant difference between men and women in their perception of ASCVD risk, with women thinking that their risk was higher compared with men (Pearson's chi-square $p=0.019$). There was a significant difference between primary and secondary prevention patients, with more concern for ASCVD risk in the secondary prevention group ($p<0.001$). No sex difference within these two groups was observed. When patients were separated according to median age (58y), the risk of ASCVD was perceived to be higher in the young patients ($p=0.003$).

Conclusion:
Overall, FH patients were concerned about their ASCVD risk, especially women. Age and a personal history of ASCVD makes a clear difference in the perception of risk for both men and women with FH.

43 - Sex-specific responses revealed during post-surgery recovery in mice fed the New Total Western Diet

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Background:
More than 38 000 cardiovascular surgeries are performed annually in Canada, with up to 25% of patients readmitted for serious adverse events. Among the predictors for readmission risk is frailty which is influenced by age and poor diet/malnutrition. Sex is also thought to contribute to readmission risk, but the underlying mechanisms behind these differences remain to be fully elucidated. To investigate the interplay between age, sex and malnutrition, we fed aged male and female mice the *New Total Western Diet* (NTWD). This diet reflects the macro and micronutrient intake of the median (50^{th} percentile) of Americans identified in the National Health and Nutrition Examination Survey (NHANES). We hypothesized that this model would better represent the patient population and provide critical insight into sex-specific outcomes after cardiac surgery.

Methods:
Retired breeder (>8 months old) male and female mice were fed the NTWD (15.5% protein, 50% carbohydrates, 34.5% fat kcal, 256g/kg sucrose, 7g/kg sodium) for 4 weeks prior to permanent left anterior descending coronary artery ligation (myocardial infarction, [MI]), sham surgery or no surgery. Surgical recovery was monitored daily using a surgery recovery matrix (SRM). Three days post-surgery, cardiac function and remodelling were assessed by echocardiography, and cardiac infiltration of immune cells was assessed by flow cytometry.

Results:
After 4 weeks on the NTWD, male mice experienced an ~9% gain in body weight, whereas female mice did not, despite female mice consuming more chow per day than males (~3.4 vs 3.1g/day). Post-surgery, male mice displayed a higher mortality rate (45 vs 27%), worse SRM scores and more substantial weight loss (12 vs 9 %) than female mice. Post-MI Male and female mice exhibited similar cardiac remodelling with comparable increases in the left-ventricle area in diastole (19 vs 21%) and systole (48 vs 54%) compared to control mice. In contrast, female mice had worse cardiac impairment (a 59% decline in the fractional area change compared to 38% in males) after MI. Both male and female mice had significant cardiac influxes of neutrophils, macrophages and LY6c high monocytes after MI. However, the differences tended to be more robust female mice.

Conclusion:
Male mice experience weight gain on the NTWD and are frailer, whereas female mice have a greater cardiac impairment and influx of immune cells. Future work will investigate if sex-specific differences in the gut microbiome contribute to differential outcomes in hopes of identifying a modifiable target for future risk mitigation strategies.

32 - Monogenic Causes of Aortic Valve Stenosis in the Quebec Population

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Background:
Aortic valve stenosis (AS) is a severe disease affecting 2 to 5% of the North American population over age 65. Typically viewed as a polygenic condition, monogenic causes of AS have not been studied in the general population. The present study aims to identify genetic variations with a strong impact on AS in the Quebec population, which is genetically unique due to a small pool of original French colonisers, creating a founder effect.

Methods:
Whole exome sequencing data from 310 AS patients of French-Canadian ancestry were analyzed. Variants were scored based on their predicted pathogenicity, minor allele frequency , and involvement in other diseases with similar phenotypes using the Exomiser software. The European portion of two datasets were then queried for the presence of high-scoring variants: the UK Biobank (415,346 participants, exome sequencing data) and the Quebec-based CARTaGENE cohort (11,587 participants, genotyping data). The association with AS of available variants in these datasets was assessed using logistic regression (adjusted for age and sex).

Results:
A total of 722 variants found in the AS patients passed our score thresholds. Of these, 369 and 541 were present in the CARTaGENE and UK Biobank data respectively. 13 and 29 variants in the respective datasets were also nominally associated with AS ($p < 0.05$). One missense variant (rs368711105) in the elastin gene (*ELN*) was associated with AS in both the CARTaGENE (p=0.023, OR=11.95) and UK Biobank (p=0.014, OR=10.80) cohorts, and two additional genes each contained at least one associating missense variant in each of the two cohorts (myosin heavy chain (*MYH7)* rs149193520: p=0.0065, OR=5.23, rs200939753: p=0.0064, OR=50.53; titin *(TTN)* rs190041566: p=0.016, OR=15.46, rs200843338: p=0.022, OR=33.65).

Conclusion:
These results support a potential role for elastin, myosin heavy chain, and titin in the development of AS, as well as point to monogenic causes of AS in a small subset of patients. Each of the identified genes has been previously associated with cardiomyopathies or vasculopathies. Future work will attempt to identify the mechanism underlying these novel genetic associations and seek to identify further Quebec-specific variants related to AS in additional patients.

51 - Cardiac surgery induces sex-specific alterations in the gut microbiome that may hamper post-surgical recovery through a proinflammatory immune response

Eszter Pal[1, 2], Lorraine Chalifour[1, 2], Yao Lu[3], Ken Dewar[4], Jeff Xia[5]

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Introduction:
Cardiac surgeries are among Canada's top ten most common surgical procedures, with serious complications requiring hospital readmission arising in up to 25% of cases. Besides the physical stress of surgery, antibiotic use, malnutrition/fasting, and older age can further predispose patients to disruptions in gut microbiome composition and function. The intestinal microbiome works in tandem with the host's immune defenses to combat infections, performs various essential metabolic functions, and ultimately, maintains host homeostasis. Disruptions in this balanced microbial community have been linked to cardiovascular disease, cardiac inflammation, as well as systemic inflammation. We propose that cardiac surgery induces alterations to gut microbial composition that may contribute to negative post-surgical outcomes through the promotion of a proinflammatory immune response.

Methods:
Gut microbiome profiles of retired breeder male and female C57bl/6N mice recovering from sham surgery or permanent left anterior descending coronary artery (LAD) ligation were temporally distinguished through 16S rRNA amplification of fecal DNA. Immune cell profiles of the heart and small intestine were characterized using flow cytometry analysis and echocardiography was performed on the day of euthanasia to assess cardiac remodeling and wound healing.

Results:
Community profiling and differential abundance analyses using MicrobiomeAnalyst revealed significant dissimilarities in baseline microbiome composition between sexes and significant microbiome remodeling post-surgery in both males and females. We observed sex-specific shifts in *Firmicutes* and *Bacteroidetes* ratios as well as microbial profiles mirroring those associated with intestinal inflammatory diseases, such as those abundant in *Proteobacteria*, *Verrucomicrobia*, and *Deferribacteres*. Flow cytometry analyses show an acute expansion of inflammatory cells and immunopathological T cells (such as TCR$\gamma\delta^+$ T cells) that is more aggressive in males and delayed in females. Echocardiography shows substantial damage to cardiac function and structure, as assessed by fractional area change (FAC), pulmonary velocity time integral (PV VTI), and left ventricle area at systole and diastole, which is similarly delayed in females.

Conclusion:
Ultimately, we characterize proinflammatory immune responses associated with cardiac surgery-induced alterations in the gut microbiome which may delay wound healing and hamper recovery. We demonstrate that biological sex plays a key role in establishing a baseline gut microbiome profile and show major sex-specific differences in post-surgical response, such as a more aggressive inflammatory response in males resulting in worse cardiac outcomes.

39 - Cardiac Resynchronization Therapy in Heart Failure and Atrioventricular Heart Block

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Background:
We aimed to assess (1) any changes in guidelines for cardiac resynchronization therapy (CRT) in heart failure and AV heart block, (2) the cost and budget impact of CRT use at the McGill University Health Centre (MUHC), and (3) local evidence on the use of CRT at the MUHC

Method:
We searched for relevant health technology assessment (HTA) reports and clinical guidelines for CRT in heart failure and AV block patients published between 2016 and 2021. We obtained information from the MUHC Electrophysiology team on the current use and costs of CRT at the MUHC.

Results:
TAU breakdown its recommendations based on the updated clinical guidelines. CRT was Approved for (1) heart failure patients with NYHA class II- IV ambulatory with LVEF ≤ 35%, QRS ≥ 150 msec, and LBBB morphology; (2) high degree AV block patients with reduced ejection fraction regardless of NYHA class who have an indication for ventricular pacing; (3) symptomatic atrial fibrillation patients with reduced ejection fraction (HFrEF <40%) regardless of QRS duration where atrioventricular junction ablation is planned. CRT is Approved for Evaluation for atrial fibrillation patients other than the above criteria.

CRT was Not Approved for (1) heart failure patients with NYHA class I, irrespective of QRS duration and morphology, or QRS duration < 130 msec, irrespective of NHYA class and QRS morphology: (2) AV block patients with normal or preserved LVEF (≥ 50%).

At the MUHC, the procedure times have decreased with greater experience over the years. The number of implantations has remained relatively stable, with a decrease during the COVID-19 pandemic. The average total cost per initial implant substantially decreased compared to the 2014/2015 fiscal period: the cost is currently $8,446 for CRT-P (decreased $2,627) and $13,766 for CRT-D (decreased $9,241).

The CardioReport information system has been acquired to prospectively collect patient data but has not been installed yet in the electrophysiology lab. Administrative data have been reported to the provincial government.

Conclusion:
CRT is recommended for the treatment of heart failure and AV block for patients with clinical criteria known to influence outcomes. For patients falling outside of current guidelines, inclusion in future clinical trials or a local database to facilitate the collection of clinical data is recommended.

50 - Generation of High-Resolution CMR Images using Deep Learning Approaches

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Background:
Cardiovascular magnetic resonance (CMR) imaging is commonly used to evaluate various conditions, such as dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM). Obtaining a precise diagnosis relies on detailed information acquired from high-resolution images, which may be challenging due to artefact and other external factors. The super resolution generative adversarial network (SRGAN) is a deep learning (DL) technique that enhances the quality and resolution of low-resolution images, specifically in the case of CMR. Transfer learning is an approach that can supplement the limited training dataset with generated images from the SRGAN model, which can enhance the quality and resolution of CMR images and enable more accurate diagnoses. This study aims to combine SRGAN with transfer learning to improve the diagnosis of different types of cardiovascular diseases using CMR.

Methods:
We assessed the super-resolution method for disease classification by comparing transfer learning models with and without super-resolution images using Python, TensorFlow, and Keras frameworks. The publicly available, Automated Cardiac Diagnosis Challenge (ACDC) dataset provided the source data for the SRGAN model, which was split into 70% training and 30% validation sets. In total, we included CINE images from 50 participants (20 normal and 30 abnormal cases: 20 DCM+10 HCM). To evaluate the SRGAN, we use the Fréchet Inception Distance (FID) metric to measure the similarity between real and generated images. Lower scores indicate greater similarity. Additionally, the Peak Signal-to-Noise Ratio (PSNR) is commonly used to assess image quality (Values <20 decibel = distortion, >30 decibel = good quality). Generated high-resolution images were used as input for transfer learning to classify different cardiac conditions. A pre-trained Visual Geometry Group 16-layer Convolutional Neural Network (VGG-16 CNN) was then fine-tuned on the generated high-resolution images to improve the accuracy of image classification.

Results:
The statistical validity of the SRGAN's performance was confirmed through the measurements of FID (357.3) and PSNR (29.99). The overall accuracy of the model was 97%, with 100% sensitivity, 94% precision, and 96% recall to classify between normal and abnormal cases.

Conclusion:
In this study, we applied DL to generate high-resolution CMR images from low-resolution inputs. Combining transfer learning with SRGAN improves the accuracy of disease classification and may potentially be applied in routine clinical practice.

38 - Temporal Trends in Frailty over a Decade of Transcatheter Aortic and Mitral Valve Procedures

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Background:
Transcatheter Aortic Valve Replacement (TAVR) indications have expanded over the years from patients with prohibitively high surgical risk to those with low risk. We sought to assess whether the prevalence of frailty among TAVR patients changed with the evolving eligibility spectrum and if it was comparable between TAVR and Transcatheter Mitral Valve Repair (TMVr).

Methods:
We performed a post hoc analysis of 405 patients (mean age 81.0±7.2, 44% females) who underwent TAVR or TMVr at McGill University Health Centre from 2013 to 2021. Frailty was measured using the Fried phenotype before the index procedure. Ordinal logistic regression was used to determine the association between calendar year and patient frailty after adjusting for age, sex, and Charlson Comorbidity Index.

Results:
The mean Fried score (and frailty prevalence) in TAVR patients was 1.8±1.2 (26.0%) from 2013-2015, 1.4±1.2 (18.4%) from 2016-2018, and 1.2±1.0 (9.8%) from 2019-2021, with an annual 0.13-point reduction (95% CI -0.21 to -0.05; P=0.002). The decline in frailty scores was independent of age and comorbidity scores, which remained fairly constant throughout, while the STS (Society of Thoracic Surgeons) predicted risk of mortality declined from 4.9% to 4.0%. The mean Fried score was similar between TAVR and TMVr (1.3±1.1) when matched for calendar years.

Conclusion:
Expanded indications for TAVR in lower risk patients have been associated with a decreasing prevalence of frailty from 1/4 initially to now 1/10, approaching the general population prevalence in this demographic. Similarly, for TMVr a growing group of older non-frail patients is being referred.

29 - TRPM7 DEFICIENCY AFFECTS CARDIAC FIBROBLASTS ACTIVATION PHENOTYPE AND CONTRIBUTES TO CARDIOVASCULAR FIBROSIS INDUCED BY ALDOSTERONE-SALT

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Introduction:
TRPM7 is a channel permeable to Mg^{2+} and Ca^{2+} bound to alpha-kinase with essential role in cell homeostasis. Hyperaldosteronism is associated with Mg^{2+} wasting. Here, we investigate the importance of TRPM7-Mg^{2+} in hypertension and fibrosis induced by aldosterone-salt.

Methods:
Wild-type (WT) and TRPM7-deficient (M7+/Δ) mice were 4-weeks treated with aldosterone (600µg/Kg/day) plus NaCl (1% in drinking-water). Blood pressure (BP) was evaluated by tail-cuff. Molecular mechanisms were investigated in cardiac fibroblasts (CF). Ca^{2+} influx was assessed by fluorescence microscopy. Intracellular [Mg^{2+}], proliferation and cell size were assessed by FACS. Protein expression was assessed by western-blot.

Results:
M7+/Δ mice exhibited reduced TRPM7 expression (30%), phospho-TRPM7 (62%) and tissue [Mg^{2+}] (28%). Levels that were recapitulated in WT-aldo-salt. M7+/Δ mice exhibited increased BP by aldo, salt and aldo-salt (135-140mmHg). In WT, only aldo-salt increased BP(134mmHg). Aldo-salt increased cardiac collagen in M7+/Δ mice (68%) and expression of IL-6, TGFβ, p-Smad3 and p-ERK1/2 (1.5-1.8 fold). CF from M7+/Δ mice exhibit reduced calcium influx induced by aldosterone (peak-response 105±0.7) vs WT:149±10. [Mg^{2+}] was reduced in CF from M7+/Δ mice (fluorescence: 1505±28 vs WT:3428±57), which was further reduced by aldosterone (20%). CF from M7+/Δ exhibited reduced proliferation (30%), increased cell size (25%) and expression of TGFβ, IL-6, p-Smad3 and p-ERK1/2 (1.4-2.0 fold) vs WT. Mg^{2+} supplementation normalized intracellular [Mg^{2+}], cell proliferation, cell size and protein phosphorylation in M7+/Δ CF($p<0.05$).

Conclusion:
Our findings identify a protective role of TRPM7 in aldosterone induced cardiovascular injury, which when downregulated, facilitates cardiac fibrosis by changing fibroblast activation phenotype through Mg^{2+} -dependent mechanisms.

31 - Docetaxel effects on lipid metabolism and atherosclerosis

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Background:
High-density lipoprotein (HDL) particles are generated in the process of removing excess cellular cholesterol. Accumulation of cholesterol in arteries is an underlying cause of atherosclerosis, and thus the HDL biogenic process has been extensively studied to reduce atherosclerosis. We have recently identified that desmocollin 1 (DSC1) negatively regulates the HDL biogenic process and that docetaxel (DTX) can inhibit the DSC1 action. Here, we have investigated if DTX can reduce atherosclerosis in mice fed a high-fat diet.

Methods & Results:
ApoE$^{-/-}$ mice fed a high-fat diet were divided into three groups after two weeks on the diet: baseline, DTX-treated and vehicle-treated groups. The baseline group consisted of mice sacrificed after two weeks on the high-fat diet. For the other two groups, we performed subcutaneous implantation of osmotic pumps in mice to administer 1 ug/ul of DTX or vehicle, respectively. These mice were fed with the diet for additional six weeks before sacrificing them to analyze the effects of DTX in lipid metabolism and atherosclerosis. The DTX treatment reduced the levels of triglycerides, non-esterified fatty acids, glucose, total cholesterol, low-density lipoprotein (LDL) cholesterol and HDL cholesterol in the blood. The DTX treatment decreased cholesterol levels in all lipoproteins but increased the HDL cholesterol/total cholesterol ratio, which is consistent with DTX promoting HDL biogenesis. In support of the circulating lipid levels, DTX decreased lipid accumulation in the liver. These improvements in lipid metabolism resulted in athero-protection: atherosclerotic lesions developed in the vehicle group were significantly reduced in the DTX group.

Conclusion:
The results show that DTX decreases atherogenic lipids (triglycerides, LDL cholesterol and total cholesterol), while increasing the HDL cholesterol/total cholesterol ratio in the blood. This athero-protective lipid profile is also reflected by reduced lipid levels in the liver and the aorta. We suggest that DTX may be used to treat atherogenic dyslipidemia and atherosclerosis.

4 - Endometriosis and Raynaud's Syndrome: A Population-Based Study in 12 Million Patients

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Background:
Raynaud's syndrome, also known as Raynaud's phenomenon is a condition caused by the spasm of small arteries and consequently, a decrease in blood flow to end arteries. A wide variety of diseases including connective tissue disorders, obstructive disorder, and eating disorders have been associated with Raynaud's syndrome. To date, there is a paucity of information about the associations between Raynaud's syndrome with endometriosis.

Objective:
Our study focused on evaluating the associations between Raynaud's syndrome with endometriosis among women registered in Healthcare Cost and Utilization Project (HCUP) database between 2007 and 2014.

Study design:
This study was a retrospective population-based survey involving 12,684,067 hospitalized women aged 18-55 years old in the US. We estimated the prevalence of Raynaud's syndrome and endometriosis. Univariable and multivariable logistic regression analyses were done to evaluate the associations between Raynaud's syndrome with endometriosis.

Results:
Of a total 12,684,067 hospitalized women included in our study, 94,891 had endometriosis and 15,799 had Raynaud's syndrome. Univariable analysis revealed a strong association between endometriosis without chronic pain with the Raynaud's syndrome (OR=1.572 95%CI: 1.356-1.822 P<.001). In the multivariable analysis, endometriosis without chronic pain still had a significant association with Raynaud's syndrome (OR=1.195 95%CI: 1.018-1.402 P=.030) after adjusted for age, race, income, type of insurance, hypertension, anxiety, and depression. Nevertheless, we could not establish the temporal causal association between endometriosis and Raynaud's syndrome because HCUP is a cross-sectional database. Moreover, the severity of endometriosis and the treatment received by the patients were not available in the database. Hence, we could not adjust for these potential confounding factors.

Conclusion:
Our study suggests associations between Raynaud's syndrome and endometriosis. This supports the postulation that endometriosis is a systemic inflammatory condition leading to endothelial dysfunction and affecting the vascular system. Further investigation on this subject is required. We recommend comprehensive evaluations including endometriosis of patients with Raynaud's syndrome or cardiovascular disease.

18 - Homozygous Familial Hypercholesterolemia in Canada: An Observational Study

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Background:
Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disease characterized by very high levels of LDL-C. Untreated patients present with extensive xanthomas and premature atherosclerosis. Lipid-lowering therapy is highly efficacious and has dramatically increased life expectancy of HoFH patients. The aim of the study was to obtain a comprehensive registry of HoFH in Canada, known to have several founder effect regions, and describe the clinical characteristics and cardiovascular outcomes of this population over time.

Methods:
Clinical and genetic data on HoFH patients were collected via a standardized questionnaire sent to academic sites participating in the FH Canada network.

Results:
A total of 48 patients with HoFH were enrolled. Median age at diagnosis was 12 years (IQR 5-24) and untreated LDL-C levels were 15.0 mmol/L (IQR 10.5-18.6). At last follow-up visit, median age was 40 years (IQR 26-54). Treated LDL-C levels were 6.75 mmol/L (IQR 4.73-9.51) with 95.5% of patients on statins, 88.6% on ezetimibe, 34.1% on PCSK9 inhibitors, 27.3% on lomitapide, 13.6% on evinacumab, and 56.8% were treated with LDL apheresis or plasmapheresis. Deaths were reported in 7 (14.5%) and major adverse cardiovascular events were observed in 14.6% of patients with the average onset at 30 years (IQR 20-36). Aortic stenosis was reported in half the patients (47.9%) and 10 (20.8%) underwent aortic valve replacement.

Conclusion:
This HoFH patient registry in Canada will provide important new health-related knowledge about the phenotypic manifestations and determinants of cardiovascular risk in this population, allowing for closer examination of quality of life and burden to the healthcare system.

13 - A Mediation and Moderation Analysis of the Effect of Maternal Hypertension and Maternal Mental Illness on Adverse Neonatal Outcomes: A Population-based Retrospective Study in 9 Million Pregnancies

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Background:
While maternal mental disorders and hypertensive disorders of pregnancy (HDP) can coexist, the impact these conditions have on neonatal outcomes is unclear. We aimed to evaluate the prevalence as well as associations and potential mechanisms between HDP, maternal anxiety and depression, preterm birth (PTB), and small for gestational age (SGA).

Method:
This population-based retrospective study used the Healthcare Cost and Utilization Project (HCUP) database from 2004 to 2014. Preterm birth (<37 weeks), SGA (<10th percentile for gestational age and sex), HDP, and mental disorders (anxiety and depression) were extracted using the International Classification of Diseases, Ninth Revision (ICD-9). We constructed mediation and moderation models to separately evaluate associations between maternal mental disorders, HDP, and adverse neonatal outcomes. We also used multivariable logistic regressions to establish their associations.

Results:
Among the 9,097,355 pregnant women studied, the prevalence of HDP was 6.9 %, anxiety 0.91 %, depression 0.36 %, preterm birth 7.2 %, and SGA 2.1 %. Anxiety increased the probability of having HDP (OR = 1.242, 95 % CI 1.235-1.250), and HDP mediated the association between anxiety and preterm birth (mediation effect = 0.048, p-value<0.001). Depression significantly moderated the effect of HDP on preterm birth (moderation effect = − 0.126, p-value = 0.027). Furthermore, HDP also mediated the association between anxiety and SGA (mediation effect = 0.042, p-value<0.001), but depression did not moderate the association between HDP and SGA (p-value = 0.29).

Conclusion:
Our results suggest that women with anxiety are at greater risk of having HDP, and HDP mediates the associations between anxiety and adverse neonatal outcomes. Depression moderates associations between HDP and preterm birth but not between HDP and SGA. We recommend physicians screen women early in their pregnancy for anxiety and depression to reduce downstream neonatal complications.

40 - Observing Family Engagement in Cardiovascular Critical Care

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Background:
Engaging families in care delivery is recommended by cardiovascular and critical care professional societies. However, actual family engagement practice in critical care has yet to be described. Understanding how family members engage in care is necessary in order to develop strategies to increase care engagement. Thus, the purpose of this study is to describe the current engagement practices in a cardiovascular intensive care unit (CICU).

Methods:
Family members of patients hospitalized in the Jewish General Hospital's CICU were monitored while visiting patients between September and December 2022. During each observation period, research personnel circulated through the CICU and observed the presence of family members as well as the type and amount of care engagement. The following data was collected: time of day, family presence, number of family members present per patient, observation time per patient, and type of family engagement observed. The type of family engagement observed was categorized as active family presence, communication, direct contribution to care, decision-making, or family needs.

Results:
There were 105 patients with 152 observation periods (AM, n=47; PM, n=50; evening, n=55). Seventy-five patients had one observation period, and 30 had multiple observation periods. The mean (±SD) observation time per period per patient was 161.0±47.7 minutes. Most patients (n=61; 58%) had family members visit. The mean number of family members present per period per patient was 1.3±0.6. Family members were present, on average, for 68% of the observation period. The most common types of family engagement domains were communication (n=61; 100%; mean time=74.5±39.1 minutes), active family presence (n=36; 59%; mean time=24.7±14.1 minutes), and direct contribution to care (n=35; 57%; mean time=27.8±16.1 minutes). The most common communication activity was communication with the patient (n=61; 100%; mean time=70.8±39.6 minutes). The most common active family presence activity was presence for physician rounds (n=20; 56%; mean time=23.3±10.6 minutes). The most common direct contribution to care activity was assisting with feeding behaviors (n=23; 66%; mean time=25.8±15.1 minutes).

Conclusion:
This is the first study to report direct observations of family engagement practice in a critical care setting. The data generated will inform efforts to design interventions to increase family engagement in acute cardiovascular care. Further studies are required to evaluate optimal family engagement practices to maximize positive patient- and family-centred outcomes.

16 - Gendered Social Determinants of Health and Risk of Major Adverse Outcomes in Atrial Fibrillation

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Background:
Atrial fibrillation (AF) is associated with a high risk of adverse outcomes. Social determinants of health (SDOH) are gendered (unevenly distributed between females and males) and associated with outcomes in cardiovascular (CV) diseases. However, whether SDOH are associated with outcomes in AF has not been well studied. We evaluated the associations between gendered SDOH and adverse outcomes in AF patients.

Methods:
The study population came from the European Society of Cardiology-European Heart Rhythm Association EURObservational Research Programme-Atrial Fibrillation (ESC-EHRA EORP-AF) General Long-Term Registry. Gendered SDOH included: education, living alone vs not, gender inequality index (GII) a measure of sex inequity at the country level and the subscales of the EQ-5D-5L questionnaire. The study outcome was a composite of major adverse cardiovascular events (MACE: ACS, stroke/transient ischemic attack/thromboembolism and CV mortality) and all-cause death. Each gendered SDOH's main effect was tested in multivariate logistic regressions and for interaction with sex.

Results:
The study population comprised 11,096 patients (mean age 69.2 years; 40.7% females, median [IQR] CHA2DS2-VASc score 3 [2-4]). Most participants had secondary education, did not live alone, did not smoke or use alcohol, were physically inactive, and lived in countries with gender equity. Compared with men, European females with AF were older, smoked less, consumed less alcohol, reported poorer quality of life measures and poorer health. Females were also more likely to live alone, less likely to have post-secondary education, less likely to engage in regular physical activity and reported more anxiety. In multivariate analyses, not living alone (OR:0.85;95%CI:0.73-0.996), better self-reported health (OR:0.96;95%CI:0.93-0.96) and regular exercise (OR:0.74;95%CI:0.63-0.87) were associated with a lower risk of MACE and all-cause mortality. Conversely reduced capacity for self-care (OR:1.35;95%CI:1.14-1.61) and smoking (OR:1.15;95%CI:1.00-1.32) were associated with worse outcomes. Female sex was associated with a lower risk of the outcome (OR:0.85;95%CI:0.74-0.98). Female sex interacted with GII (OR:1.15;95%CI: 1.00-1.31) indicating poorer outcomes in females living in countries with higher sex inequities.

Conclusion:
Gendered SDOH are independently associated with adverse outcomes in AF and need to be considered when risk stratifying patients with AF.

56 - IMPACT OF PHYSICAL FRAILTY ON FUNCTIONAL RECOVERY POST CARDIAC INTERVENTION IN HEART FAILURE PATIENTS

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Background:
Frailty, a condition characterized by physical vulnerability and decline, is frequently observed in older adults and is associated with an increased risk of adverse health outcomes, including heart failure. Frailty and heart failure often coexist, as frailty may increase the risk of developing heart failure and heart failure may, in turn, exacerbate frailty and necessitate surgical intervention. Despite the prevalence of these conditions, few post-cardiac interventional studies have investigated functional recovery in older frail patients with heart failure. This study aims to assess functional recovery in this population and to explore the relationship between frailty and heart failure, using the Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls (SARC-F) questionnaire to predict recovery outcomes.

Methods:
This prospective cohort study consists of 1990 patients from the McGill Frailty AVR study and frailty registry who underwent cardiac interventions for valvular heart disease. Frailty baseline scores were assessed using the SARC-F questionnaire with frailty being defined as a SARC-F score of 4 or higher. Functional recovery was assessed by comparing SARC-F scores at a 12-month follow-up to those at baseline. Multivariable logistic regression models were employed to investigate the association between frailty and functional recovery, adjusting for potential confounders including age, sex, body mass index (BMI), left ventricular ejection fraction (LVEF), NYHA class, Charlson comorbidity score, type of intervention, habitual physical activity, malnutrition, cognitive impairment, depression, and ADL disability.

Results:
231 (11.6%) patients were frail at baseline of which 109 (47.2%) demonstrated functional recovery at 12-month follow-up. The multivariable logistic regression analysis revealed that SARC-F baseline score (OR=0.73, 95%CI 0.54-0.99, p=0.04), habitual physical activity (OR=1.39, 95%CI 1.10-1.76, p=0.01) and ADL disability (OR=0.41, 95%CI 0.20-0.86, p=0.02) were significantly associated with functional recovery. Other potential confounders such as age, BMI, LVEF, comorbidities, and type of intervention did not demonstrate significant associations with functional recovery.

Conclusion:
The study highlights the significant impact of physical frailty on functional recovery post-cardiac intervention in heart failure patients, with the SARC-F questionnaire, habitual physical activity, and ADL disability being important factors in predicting recovery outcomes.

12 - Reproducibility of Oxygenation-Sensitive Cardiac Magnetic Resonance Breathing-Induced Myocardial Oxygenation Reserve Across Scan Vendors and Field Strengths

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Background:
Oxygenation-Sensitive Cardiac Magnetic Resonance (OS-CMR) is a validated tool to examine vascular function using the breathing-induced myocardial oxygenation reserve (B-MORE) (Fischer et al., 2018, Hillier et al., 2022). However, the interpretation of published B-MORE values has been limited to Siemens scanners, and the reproducibility of B-MORE values across repeated scans is yet unknown. Additionally, field strength may confound the interpretation of B-MORE values, with the contrast between normal and deoxygenated myocardium increased at higher field strengths. The aim of this preliminary study was to assess the reproducibility of B-MORE values acquired during consecutive OS-CMR scans among different scanners and field strengths.

Method:
We conducted a single-centre, retrospective study and measured B-MORE in images from 3 different scans in each subject using a vasoactive breathing maneuver, composed of a period of paced hyperventilation followed by a voluntary maximal breath hold. Scans were performed consecutively using a 1.5 T Artist (GE Medical Systems), a 3 T Premier (GE Medical Systems), and a 3 T Skyra (Siemens Healthineers). B-MORE values were calculated from the first post-hyperventilation end-systolic image and the end-systolic image closest to 30 seconds of the breath hold. Repeated-measures ANOVA was used to view differences in basal slice, mid-slice, and global B-MORE across the three scans.

Results:
We performed 24 OS-CMR scans in 8 healthy adults (4 female, mean age=42 years). B-MORE did not differ significantly due to field strength or vendor, though a trend towards lower 1.5T values was observed. Mean global B-MORE values were 9.3%, 9.0%, and 3.2% on the Siemens Skyra, GE Premier, and GE Artist, respectively. Global B-MORE results were not significantly different between the 3 scans (p=0.22) in ANOVA analysis. Mean basal B-MORE values were 9.2%, 9.3%, and 4.0% on the Siemens Skyra, GE Premier, and GE Artist, respectively. Basal slice B-MORE results were not significantly different between the 3 scans (p=0.53) on ANOVA analysis. Mean mid-slice B-MORE values were 9.2%, 9.0%, and 2.7% on the Siemens Skyra, GE Premier, and GE Artist, respectively, and were not significantly different (p=0.052) on ANOVA analysis.

Conclusion:
These preliminary results indicate that global B-MORE values are reproducible across scan vendors. Though not statistically significant, a preliminary trend of lower B-MORE values at 1.5T, when compared to 3T values, agrees with previous research. Larger studies are necessary to examine the clinical impact of field strength-induced B-MORE variations on the ability of OS-CMR to differentiate diseased from healthy states.

1 - 3D Cardiac Magnetic Resonance Multitasking: First Clinical Experience

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Background:
Cardiac magnetic resonance (CMR) Multitasking is a novel acquisition and reconstruction method which can resolve cardiac/respiratory motions and acquire quantitative parametric mapping measurements across the entire left ventricle (LV) without the need for ECG gating or breath-holding (1). The aim of this study was to test the clinical utility of Multitasking in a mixed healthy volunteer (HV) and patient population.

Methods:
HV and patients referred for a clinical CMR exam were recruited. Exams were conducted on a 3T MR system (Magnetom Skyra™, Siemens Healthineers, Erlangen, Germany). 2D balanced steady-state free precession (bSSFP) images were acquired in the in 2-chamber, 3-chamber, 4-chamber views, and as a short axis stack (SAX) through both ventricles. A standard T2-SSFP sequence was used to acquire 6 SAX T2 maps. The Multitasking sequence was used to acquire a 3D stack of SAX cine and T2 mapping images. Multitasking images were reconstructed using a low rank-tensor framework and then used for LVEF and T2 quantification (1). All data were analyzed using certified software (cvi42, Circle Cardiovascular Imaging Inc., Calgary, AB, Canada). The LVEF was calculated from SAX images. Bland-Altman analyses were used to compare LVEF measurements between Multitasking and bSSFP images. The HV were used to create sequence-, scanner-, and site-specific T2 normal values. A chi-squared test was used to compare the similarity of disease classification between T2-SSFP and Multitasking in patients.

Results:
21 patients (mean age 55y., 11 male) with mixed pathologies (Table 1) and 20 HV (mean age 39y., 10 male) were recruited for this study. Multitasking underestimated LVEF with an average difference of 5% compared to bSSFP measurements (Fig. 1A). Multitasking T2 measurements were lower than T2-SSFP on average (Fig.2A and 2B) with larger standard deviations in all AHA segments (Fig.2C and 2D) of the HV cohort. However, in patients Multitasking demonstrated strong agreement with T2-SSFP in classifying AHA segments as having elevated or normal T2 values ($p = 0.04$) (Figure 2E).

Conclusion:
This study shows the potential clinical use of Multitasking to quantitatively assess LVEF and T2 in various clinical pathologies at 3T without breath-holding or ECG triggering. Multitasking T2 values measured with higher variability compared to the standard T2-SSFP sequence but was able to correctly classify pathology in 85% of patient cases. Although further adjustments are required to decrease the variability in T2 measurements, this acquisition strategy may have clinical value in patients with trouble holding their breath or in pediatric populations.

5 - Association of Earlier Menopause with Myocardial Remodelling: A Cardiovascular Magnetic Resonance Imaging Study

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Background:
Sex differences in cardiovascular disease (CVD) have been increasingly recognized, where females may have specific factors that may influence CVD risk. Early onset menopause is associated with a higher incidence of CVD and randomized trials testing exogenous hormonal therapy have been conducted with the aim of reducing this risk compared with females who had naturally occurring menopause at age 50-51 years, those with premature (younger than 40 years) and early menopause (younger than 45 years) and subsequent deficiency of circulatory 17 beta-estradiol (E2) have an increased risk for adverse events, including heart failure and mortality, before the age of 60. We aim to assess the effect of early menopause on cardiac function, longitudinal strains, and tissue characteristics using cardiac magnetic resonance imaging (CMR).

Method:
A total of 44 participants- without previous history of CVD- who underwent CMR were classified into 2 groups: earlier menopause (n=22) and aged-matched healthy group with naturally occurring (regular) menopause (n=22). Demographic and CMR data of all participants were collected. Statistical analysis was performed using Microsoft Excel statistical software 2016 (Baton Rouge, United States). The data was verified for the normal distributions. Categorical data are expressed as percentages and continuous variables as mean± SD. For the comparison of two parametric variables, the unpaired t-test was used. A p-value of less than 0.05 was considered statistically significant.

Result:
Mean age of the participants in the earlier and regular menopause groups was 55.8 ± 8.36 and 55± 9.1 years, respectively (p value= 0.74). The age of menopause onset in the earlier group was 39.8±5.8 years and regular menopause was 50.9± 4.27 years (p value<0.001) (Table 1). In females with earlier menopause, T1 mapping values (1223.4± 48.52 seconds) were significantly higher, compared to those with regular menopause (1181.9± 38.04 seconds) (p value= 0.003) (Figure 1, A). The mean global T2 values, in females with earlier menopause (47.5± 5.69 seconds) were significantly higher than in females with regular menopause group (43.7± 4.42seconds) (p value= 0.0311) (Figure 1, B). There were no significant differences between left ventricle ejection fraction, global longitudinal strain, and maximum left atrium volume in both groups (p values= 0.22, 0.16, and 0.31, respectively) (Table 1).

Conclusion:
In females with earlier menopause- lack of the cardioprotective endogenous E2- abnormal alterations in myocardial tissue characterization are present that are not evident in females with regular menopause. These subclinical findings may be one mechanism linking premature cardiovascular disease to menopause.

17 - Deep Transfer Learning for the Automated Assessment of Sarcopenia and Body Composition using Clinical Cardiac Magnetic Resonance Scans

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Background: Sarcopenia, defined as age-related loss of muscle mass, is a risk factor for mortality and morbidity in patients with cardiovascular disease. Methods to quantify muscle mass are not always available in clinical workflows, however, cardiac magnetic resonance (CMR) provides axial imaging of the thorax that can be examined to assess body composition.

Methods: We assembled a retrospective cohort of adult patients that underwent clinically indicated CMR at two centers. We extracted the axial black-blood HASTE images as acquired on 1.5T and 3T Siemens scanners, with approximately 20 slices spanning the entire thoracic cavity. We manually segmented the skeletal muscle and subcutaneous fat tissues in a representative subset of 30 patient CMR scans (570 axial slices) and then used these segmentations to re-train a DL model previously validated in >1,000 patient CT scans ("transfer learning"). The final DL model was based on the U-Net structure with 4 skip connections and 17.2M parameters; trained using the Adam optimizer with a cross-entropy and Dice loss function. Thoracic skeletal muscle volume was indexed to body surface area (iSMV).

Results: A total of 1321 CMR scans were analyzed. Ten-fold cross-validation yielded 0.946 average accuracy on the validation set, we used the best fold with 0.953 accuracy to perform inference on these scans. The median iSMV was 1431 cm3 (IQR 1300, 1591) and 1111 cm3 (IQR 994, 1231) in men and women with evidence of heart failure as compared to 1542 cm3 (IQR 1420, 1699) and 1130 cm3 (IQR 1035, 1239) in men and women without heart failure. Low iSMV was associated with advanced age (-4 cm3 per year, 95% CI -5 to -3), female sex (-329 cm3, 95% CI -418 to -367), and a primary diagnosis of heart failure (-46 cm3, 95% CI -74 to -18) in a multivariable linear regression analysis.

Conclusion: Quantification of muscle mass can be rapidly automated from clinical CMR scans using a DL transfer model. Cardiovascular disease, in particular heart failure, is confirmed to be associated with the phenotype of sarcopenia.

24 - Vascular smooth muscle cell phenotype switching in human hypertension is Nox5-dependent

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Background:
Reactive oxygen species (ROS) play a key role in vascular smooth muscle cells (VSMCs) phenotypic switching in hypertension. Nox5 is a major ROS generating enzyme in vascular cells and is upregulated in VSMC in hypertension. However, the effects of Nox5-derived ROS on VSMC proteome and phenotype in human hypertension are unknown. We aimed to characterize the global and oxidative proteome profile of VSMC and the role of Nox5 on VSMC phenotype in human hypertension.

Method:
Using high fidelity proteomic analysis, we characterized the proteome of VSMC in human hypertension. VSMC from resistance arteries from normotensive (NT) and hypertensive (HT) subjects were studied. Proteins were labelled with isobaric tandem mass tags and identified by liquid chromatography tandem mass spectrometry. The oxidative proteome was assessed using stable isotope-labelled iodoacetamide to target cysteine thiols. Nox5 silencing was performed by siRNA. Protein expression was assessed by western blotting. Pro-inflammatory cytokines (IL-6, IL-8) and pro-collagen I were detected in VSMC culture medium by Elisa.

Results:
The proteomic analysis identified 207 proteins upregulated in HT (fold change>1.5, $p<0.05$). Gene ontology enrichment of upregulated proteins in HT showed that most proteins belong to extracellular space and plasma membrane compartments and were involved in biological processes such as extracellular matrix organization, immune response and cell proliferation. Extracellular matrix (ECM) proteins COL1A1, COL9A1, COL10A1, FBN1, FBLN1 were increased in HT subjects, suggesting a switch to a fibroblast-like phenotype in hypertension. Expression of proteins related to the interferon and IL-1β pathways (IFIT1-3, MX1-2, IL1RAP, CD36, ICAM1) were also increased in cells from HT subjects. The oxidative proteome analysis identified 130 significant cysteine-containing peptides, 88 showed increased oxidation in HT (fold change>1.5, $p<0.05$). Among the highly oxidized proteins in HT were ECM proteins, COL11A1, COL16A1, FBLN1 and FBLN2. In HT subjects, expression of VSMC markers myocardin, α-smooth muscle actin (α-SMA) and smooth muscle specific protein SM22 were reduced ($p<0.05$) while expression of proliferation marker, PCNA and pro-collagen I were increased ($p<0.05$). Pro-inflammatory cytokines IL-6 and IL-8 release was increased in HT ($p<0.05$). Nox5 silencing in HT subjects reduced PCNA expression, pro-collagen I release, baseline and LPS-induced IL-6 and IL-8 release ($p<0.05$). Furthermore, Nox5 silencing increased expression of myocardin, α-SMA and SM22 in HT subjects.

Conclusion:
Our study provides new insights into the proteomic changes related to vascular phenotype in hypertension and demonstrated that Nox5 play an important role in VSMC phenotypic switching associated with vascular injury and remodelling in hypertension.

30 - Establishing a reliable in vitro model of doxorubicin-induced cardiotoxicity

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Background:
Doxorubicin (Dox) is the most common chemotherapy drug used to treat hematological and solid tumours in patients. However, Dox is well-known to promote doxorubicin-induced cardiotoxicity (DIC), posing the most significant risk for cancer survivors to develop irreversible cardiac dysfunction and heart failure after treatment. Unfortunately, various models of cardiotoxicity *in vitro* lack reproducibility, since cardiomyocytes are terminally differentiated, and it is difficult to perform high-throughput experiments while accounting for patient variability. To develop novel therapies, a personalized and more accurate cellular model is necessary to understand the mechanisms which lead to DIC. This project utilizes induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) to develop a robust Dox injury model to mimic what occurs *in vivo*. This will allow us to elucidate the cellular processes that contribute to Dox sensitivity in patients.

Methods:
First, iPSC-CMs were generated from peripheral blood of healthy donors as well as cardiomyopathic and DIC patients, using established reprogramming and differentiation protocols. **Second**, we induced proliferation in iPSC-CMs by following a protocol developed by Mass et al. (2021) whereby 2μM CHIR was added to the media of passaged iPSC-CMs. At different passages, iPSC-CMs were characterized via immunofluorescence. **Subsequently**, iPSC-CMs were treated with increasing/varying Dox concentrations (0, 0.1, 0.05 and 1) over 24, 36 and 48h to determine the optimal concentration of Dox to mimic DIC. Pre- and post-Dox treated iPSC-CMs were compared using Crystal Violet and AlamarBlue, to determine viability and metabolic activity.

Results:
The application of 2μM CHIR in RPMI/B-27 supplement plus insulin has shown a significant increase in the number of iPSC-CMs after replating them (2-4-fold expansion). When characterizing iPSC-CMs, we confirmed the expression of cardiac markers GATA4, SERCA2a, TNNT2, CX43. When incubating iPSC-CMs with Dox, we found significant decreases in viability and metabolic activity ($p<0.01$), when comparing 36h and 48h incubations to 24h, and increasing Dox concentrations, observing a concentration-dependent effect.

Conclusion:
We identified the optimal conditions to induce DIC *in vitro*, with 0.05-0.1μM Dox incubated for 48h. Furthermore, we validated an approach for expanding iPSC-CMs, which is a novel method to generate a high throughput cardiotoxic injury model. In the long term, this would allow for **1)** patient stratification with regards to Dox sensitivity and **2)** the development of novel therapies to prevent DIC for already-affected patients. This project paves the way for the study of patient-specific susceptibility to Dox injury, ultimately translating to a clinical impact and improving cancer and cardiovascular outcomes.

25 - Cardioneural Ablation for Vasovagal Syncope: An experience from McGill University Health Center

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Background:
Cardioneural ablation (CNA) is a novel catheter-based technique to treat patients with clinically significant bradyarrhythmia due to a cardio-inhibitory subtype of VVS. The aim of this study is to demonstrate the efficacy and safety of this procedure.

Methods:
Data was collected prospectively for all patients undergoing CNA between December 2020 to the present. Patients were required to have a history of recurrent traumatic syncope, refractory to medical management and to have an implantable loop recorder (ILR) to document prolonged pauses correlating with syncope. CNA was performed under general anesthesia with a 3D mapping system. Left atrial access was obtained through transseptal puncture, and an ablation catheter was used to identify fragmented signals in anatomical regions consistent with ganglionic plexi (GPs). High frequency stimulation (60ms at 20mV for 4 seconds) was delivered at sites of interest in both the left and right atria. Prolongation of the R-R interval by 50% was used to confirm GP location. Loss of positive response to high-frequency stimulation was used to confirm successful ablation in addition to loss of capture. Radiofrequency energy was delivered (target ablation index of 400) with a vagal response noted. This method of high frequency stimulation, ablation, and repeat stimulation was repeated at each of the known GP sites.

Results:
Between December 2020 and December 2022 four patients with medically refractory cardio-inhibitory syncope underwent CNA. All patients had objective adjudication of their outcomes through remote and in-clinical follow-up of their ILRs. Mean age was 28.5±5 years, mean syncopal episode per patient 9.3±1.2 pre CNA. Baseline heart rate under GA was 63.5+-12.99bpm and 87.5±6.08 after the ablation. Baseline PR pre 204±59.89ms and post 172.6±21.93ms. Mean procedure time was 93.5±9.1 minutes. During a mean follow-up 10±3.19 months, 3 patients remained asymptomatic and one patient required a repeat limited ablation due to a syncope recurrence 7 months post-ablation. There were no procedure related complications and currently, all four patients remain free from syncopal event.

Conclusion:
CNA is a novel catheter-based technique that may be considered as a treatment option for recurrent VVS with a clear dominant cardioinhibitory response once general treatment measures have been attempted. The risks of the procedure may be acceptable in appropriately selected patients, particularly in younger patients, where pacemaker implantation remains the only other option. In this small cohort of patients, we demonstrate safety and efficacy at nearly 1 year follow-up. Larger studies are required to confirm these findings

34 - Methods for Pharmaceutical Drug Loading on a Multi-Walled Carbon Nanotube-Based Drug-Eluting Coating for Metallic Implants in Blood-Contacting Environments - *Abstract Retracted*

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Multi-walled carbon nanotubes (MWCNTs) are a promising medium for drug immobilization and release. While a lot of work regarding the use of MWCNTs as individual drug carriers is currently performed, the idea of employing them as a drug-loaded interface on surfaces of metallic implants, such as cardiovascular stents, is still less popular. Several methods to load pharmaceutical drugs and drug substitutes electrostatically and covalently to MWCNTs on metallic substrates have been explored. Preliminary experiments explored the potential of loading a drug substitute onto a heavily entangled MWCNT forest which was directly grown on a 316L stainless steel (SS) mesh by chemical vapour deposition. Methylene blue (MB) loading was achieved by immersion of bare and MWCNT-coated SS mesh samples in concentrated MB solutions. The electrostatic loading of MB onto the MWCNT-coated SS mesh samples was confirmed and quantified by UV-vis spectroscopy. The amount of MB loaded onto MWCNT-coated SS mesh samples was significantly higher than for bare SS mesh samples. Release experiments of the MB-loaded MWCNT samples were performed in reverse osmosis water at 37 ^{o}C while being agitated at 50 rpm and were monitored over a span of 24 hours. An initially high MB release rate was observed to decrease over time and nearly plateau after 18 hours.

The same set of experiments was performed with a pharmaceutical blood thinner. Characterization of the drug solutions after loading by UV-vis spectroscopy demonstrated that the concentration of the drug compound in the loading solutions did not decrease and that none of it was entrapped in the MWCNT coating which can be explained by the size of the drug macromolecule, unable to diffuse into the MWCNT forest. This led to the motivation to immobilize the drug compound on the MWCNT coating surface by covalent bonding. The MWCNT forest surface was functionalized by continuous, non-thermal ammonia plasma to graft amine (-NH_2) groups onto the surface. The carboxyl groups (-COOH) of drug molecules were then bonded to the -NH_2 groups on the MWCNTs using crosslinking agents. XPS spectra of the drug-loaded MWCNT samples showed the appearance of a sulphur peak which is attributable to the presence of the pharmaceutical agent. Quantification by Toluidine Blue O assay proved an average loading efficiency of 30-40%. As such, the ability to entrap or covalently bind pharmaceutical drugs and substitutes on metallic surfaces covered by MWCNTs has been demonstrated.

47 - Sex Differences in Familial Hypercholesterolemia in a single center

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Familial hypercholesterolemia (FH) is characterized by elevated Low-density lipoprotein-cholesterol (LDL-C) and elevated risk of premature atherosclerotic cardiovascular disease (ASCVD). Early recognition and treatment with statins substantially improves clinical outcomes. While men and women are equally affected, differences in the treatment of women have been previously noted. The objective of the present report is to examine the differences in treatment between men and women with FH in a single academic center using a prospective cohort study design. Descriptive analysis was used, using a T-test, Mann-Whitney U test, or Chi-squared test to find p-values. A total of 361 adult patients were followed for a mean period of approximately 10 years. It was found that women were diagnosed with FH significantly later than men, men were more likely to have coronary artery disease (CAD), and their age of presentation with CAD was significantly younger than in women. Untreated LDL-C levels were higher in men as compared to women. At the time of the initial visit, approximately 50% of patients were on lipid-lowering therapies (LLTs). Women were less aggressively treated than men, and women were also less likely to reach the goal LDL-C reduction of 50% from LLTs versus men, even after follow-up. This difference in treatment did not translate into an increase in MI, or major adverse cardiovascular events (MACE) in women versus men. This bias towards lipid lowering therapy for women needs to be addressed. Importantly, more data is needed regarding the risk of ASCVD in women in primary prevention, compared to men. Despite this being a small-scale analysis, the findings are important to be able to add to the growing discovery of sex-related differences in healthcare to be able to address the inconsistencies.

52 - Fetal sex and maternal pregnancy outcomes

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Introduction:
To date, there are still no accurate methods to predict whether a pregnancy will be affected by comorbidities such as gestational hypertension, preeclampsia, and gestational diabetes. We can help improve prediction by evaluating which factors can increase the risk of these comorbidities. Some evidence show that fetal sex could be considered a risk factor, but clinical guidelines still do not list it as one. Our objective is to extend scientific evidence on the effect of fetal sex as a risk increasing factor.

Methods:
We evaluated the effects of fetal sex over the development of primary outcomes (gestational hypertension, preeclampsia, and gestational diabetes) and secondary outcomes (APGAR scores, stillbirth, birth weight, and cesarian section). We also performed subset analysis according to (1) gestational age at delivery, (2) nulliparity versus multiparity, and (3) the number of risk factors present. The study population consisted of women at high risk of developing preeclampsia that have singleton pregnancy and a natural or an assisted reproductive therapy conception. They were recruited from the obstetrics clinics at the Royal Victoria Hospital and the Jewish General Hospital between 2013 and 2016. We obtained data through patient chart reviews and patient-filled baseline questionnaires. 197 women were included in the analysis.

Results:
We did not find any statistically significant association between carrying a male fetus and any of the pregnancy-related outcomes. However, we noticed higher odds ratio for male-bearing pregnancies to have term preeclampsia and gestational hypertension, and secondary outcomes. We saw that having a male fetus reduces the odds ratio of having gestational diabetes. We did not observe any associations when looking at pre-term deliveries except for APGAR scores. Here, the odds ratio for male neonates to have non-reassuring APGAR scores were lower. Nulliparous pregnancies with male fetuses further increased the odds ratio to have at least one form of primary outcome compared to looking at fetal sex alone. Similarly, women with at least 3 risk factors for preeclampsia carrying a male fetus had an increased odds ratio to develop at least one form of primary outcome compared to the evaluation of fetal sex alone.

Conclusion:
Although not statistically significant, a greater number of pregnancy related comorbidities are associated with male-bearing pregnancies. The odds ratio of having at least one form of primary outcome is even higher in male-bearing pregnancies when adjusted for term deliveries, nulliparous pregnancies, or women that had at least 3 risk factors for preeclampsia.

36 - Beyond the beat: predicting frailty in cardiovascular patients using LF/HF heart rate variability ratio

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Background:
Frailty reflects a state of increased vulnerability to adverse health outcomes due to age-related changes in body composition, mobility, and autonomic control. Heart rate variability (HRV) represents the time interval oscillations between consecutive heartbeats. Among the HRV parameters, the low-frequency (LF) to high-frequency (HF) ratio (LF/HF) depicts a complex balance of sympathetic to parasympathetic control and thus, a marker of cardiac autonomic regulation. The LF/HF ratio has been shown to be associated with frailty. We aimed to determine whether a similar association is seen in the cardiovascular disease (CVD) patient population and if this LF/HF ratio could be used as a surrogate marker of frailty in such patients.

Methods*:*
A cross-sectional study was conducted for adult patients visiting the ambulatory cardiology clinic at the Jewish General Hospital, McGill University. HRV was assessed at rest for 2 minutes 30 seconds using the Elite HRV CorSense monitor. Patients who were electrically paced, had atrial fibrillation, or otherwise presenting with arrhythmia at the time of visit were excluded. Frailty was assessed using the clinical frailty scale (CFS) and a CFS ≥ 5 was considered frail. A comprehensive history and physical examination were completed as per routine.

Results:
The cohort was comprised of 155 patients (66.9 ± 13 years, 68 females). The prevalence of frailty was 15% (78.6 ± 10 years, 12 females) with a median LF/HF ratio of 0.37, relative to a significantly greater LF/HF ratio of 1.01 ($p<0.001$) in the non-frail population (64.8 ± 12 years, 56 females). This difference was mediated by a rise in HF peak in the frail vs. non-frail population (0.34, 0.28, respectively, $p=0.002$). Out of all HRV parameters, the LF/HF ratio was correlated with frailty and decreased by 0.437 for each unit increase in CFS ($p<0.001$). LF/HF ratio of 0.37 most optimally predicted frailty (54% sensitivity, 82% specificity, 0.77 ROC). Adjusting for age, sex, and comorbidities did not affect the observed association between the LF/HF ratio and frailty.

Conclusion:
The LF/HF ratio demonstrates an inverse relationship with frailty, establishing itself as an effective predictive tool for identifying CVD patients who require additional evaluation for frailty. Moreover, the HRV parameters present a promising potential for monitoring frailty and interventions, however more research is necessary to fully assess their practical implementation.

23 - Sex-Differences in Stress Burden and Markers of Cardiac Inflammation —A Cardiovascular Magnetic Resonance Imaging Study

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Introduction:
Stress has been associated with the incidence of cardiovascular disease (CVD), with women experiencing nearly twice as many stress disorders in their lifetime as men. CVD is the leading cause of death in women and female-specific risk factors have helped to understand this trend further. However, whether stress is one of the mechanisms explaining increased CVD mortality and adverse prognosis in women needs further investigation. CMR is the reference standard for quantifying cardiac inflammation. Specifically, important advancements in CMR technology have allowed for high-resolution and clinically applicable quantitative T1 and T2 mapping techniques for the detection of cardiac inflammation. The present study aims to identify sex differences in the impact of stress burden, as measured by Perceived Stress Scale (PSS) scores, on markers of cardiac inflammation, in females and males.

Methods:
In this single-center prospective study, we analyzed T1 and T2 maps performed on a 3T GE scanner in patients with CVD and healthy participants who had previously completed the PSS questionnaire. PSS is a globally used and self-reported scale measuring perceived stress that exhibits strong psychometric properties with good reliability and high construct validity. All images were assessed for global values using cvi[42] (Circle CVI, Calgary, AB, Canada). Analyses were stratified by sex and PSS groups (PSS score<14: low-stress group, PSS14: higher stress group). An independent samples t-test was used to compare T1 and T2 global mean values between males and females in both low and higher stress groups. Values are reported as mean± standard deviation. Multiple linear regression analysis was used to investigate the associations.

Results:
We studied 41 patients (mean age 57.27±10.7 years, 37% females) and 21 healthy participants (mean age 50.43 ±10.9 years, 43% females). In the higher stress group (n=33, 55% females), in comparison to males, females had higher T1 (1246.2±51.2 vs. 1191.2±45.0ms; p=0.002) and T2 global values (49.02±3.8 vs 45.04±4.5ms; p=0.013) despite similar stress levels (PSS 19.67±3.7 vs 19.53±3.7) (Panel Figure). There was no such difference in the lower stress group (n=28, 21% females). A sex and age-adjusted linear regression model, with PSS scores as a covariate, significantly predicted T1 (R^2 = 0.869, p=0.017) and T2 (R^2 = 0.902, p=0.008) values.

Conclusion:
Higher stress levels have a stronger association with markers of cardiac inflammation with females than with males. This sex difference in the relationship of stress burden and inflammation may contribute to the increased CVD mortality and morbidity in females.

35 - Cumulative and time-varying effects of severe maternal morbidity on cardiovascular hospitalization

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Background:
Severe maternal morbidity (SMM) is a leading cause of maternal mortality, wherein the risk of death increases with the number of morbidities a mother experiences. SMM is also linked with future ill health, including a heightened risk of subsequent cardiovascular hospitalization. This association is highest in the first year after delivery but persists for up to 30 years postpartum. Despite this knowledge, SMM is often modeled as a time-invariant exposure, where a mother is considered unexposed until experiencing an SMM and exposed afterwards. This approach does not account for changes in the impact of SMM over time, the impact of multiple SMMs, or the impact of SMMs of varying severities. Thus, we aim to model the cumulative effect of SMM as a time-varying exposure.

Method:
Using data from the Canadian Institute for Health Information's (CIHI) national database on hospital births between 2006 and 2018, we will run Cox proportional hazards models with a weighted cumulative exposure (WCE) assessment. This WCE assessment takes into account the duration, timing, and severity of an exposure and combines them into a summary exposure metric.

We will initially develop an SMM severity scale to assign weights to individual SMM types. We will then incorporate the severity weights into the WCE assessment. We will compare results from Cox proportional hazards models with and without the WCE assessment, and between iterations of the WCE assessment.

Results:
The cohort includes 1,419,534 primiparous (index) deliveries and 1,582,690 subsequent deliveries. Among index deliveries, 1.97%, 0.22%, and 0.12% deliveries were affected by 1, 2, and 3 or more SMM types, respectively. The hazard ratio from the initial Cox regression model comparing women who experienced any SMM to women who experienced no SMM was 3.7 (3.4-4.0). Hazard ratios for 1, 2, and 3 or more SMMs in the index pregnancy were 3.1 (2.8-3.5), 6.1 (5.0-7.6), and 7.1 (5.5-9.0), respectively.

Conclusion:
Using the association between SMM in primiparous index pregnancies and cardiovascular hospitalization in our cohort, we will evaluate and optimize a novel approach for modeling SMM which accounts for variable duration, timing, and severity of SMM exposure. This research will allow for a better understanding of the impact of SMM given different patterns of morbidity exposure and will establish an SMM severity scale that will allow for more specific modeling of SMM exposure.

19 - IMPROVING THE DIAGNOSTIC CONFIDENCE OF LATE GADOLINIUM ENHANCEMENT FOR THE ASSESSMENT OF ISCHEMIC AND NON-ISCHEMIC FIBROSIS USING TI-SCOUT IMAGES

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Background:
Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) is the standard, non-invasive tool to identify myocardial scar. This method is generally used to diagnose, characterize and predict prognosis in a broad spectrum of ischemic and non-ischemic cardiomyopathies (1). LGE-CMR requires an injection of 0.1-0.2 mmol/kg of gadolinium-based contrast agent, an adequate inversion-recovery pulse to suppress signal from normal myocardium, and acquisition of T1-weighted images after a 10 to 20-minute delay. Inversion time (TI)-scout images (which use a look-locker sequence) are needed to select the optimal myocardial nulling time before acquiring LGE images (1). Since the TI-scout acquires images over a range of different inversion times, it may provide useful insight into abnormal kinetics of gadolinium-based contrast¾ as in the case of cardiac amyloidosis or provide additive information about the myocardial injury, especially in areas of the myocardium near the blood-pool interface. We assessed the value of the TI scout, in addition to LGE, for the assessment of myocardial fibrosis in patients with ischemic and non-ischemic cardiomyopathy.

Methods:
Of 133 patients, 27 (21%) had no visible enhancement in standard or TI-scout images. In the remaining 106 LGE-positive patients, the additional use of the TI-scout increased the diagnostic confidence in 16 patients (13%), including 4% of patients with ischemic cardiomyopathy. The TI-scout provided additive information about enhancement in the papillary muscles in 7 patients (6%) and the right ventricle in 3 patients (3%).

Conclusion:
Our study indicates that the additional use of the TI-scout on top of standard LGE images may improve diagnostic decision-making in patients with suspected irreversible myocardial injury.

References:
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9 - THE DIFFERENCE OF SUITABLE INVERSION TIMES FOR LATE GADOLINIUM ENHANCEMENT CARDIAC MAGNETIC RESONANCE IMAGING BETWEEN RIGHT AND LEFT VENTRICLES

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Background:
Late gadolinium enhancement (LGE) - cardiovascular magnetic resonance imaging (CMR) is an established clinical method for assessing myocardial viability. The success of this method is contingent on choosing an appropriate inversion time (TI) which nulls healthy myocardium and exposes fibrotic tissue with a bright signal intensity (1). Although the right ventricle (RV) is involved in many pathological conditions, the choice of TI is based on the time which nulls the left ventricle (LV) muscle which may be inappropriate to assess fibrosis in the RV (2-3). Our goal was to define differences between RV and LV myocardial TI.

Methods:
The TI-scout images of patients who underwent a clinically indicated CMR were retrospectively analyzed to identify the appropriate TI of both the RV and LV by two experienced clinical readers. The CMR exams were completed on one of three scanners: a 1.5T Artist(GE Healthcare, Milwaukee, USA), a 3T SIGNA Premier (GE Healthcare, Milwaukee, USA) or a 3T Skyra (Magnetom Skyra™,Siemens Healthineers, Erlangen, Germany). A sub-analysis was conducted on hypertrophic cardiomyopathy (HCM) patients with a thickened RV wall to rule out the influence of partial volume averaging (with the blood pool or epicardial fat) on differences in TI between the RV and LV.

Results:
133 patients (mean age = 53.6± 16.9 years, 63.2% male) were enrolled into this study: 73% non-ischemic cardiomyopathy, 23% ischemic cardiomyopathy and 4% non-specific cardiomyopathy.

62% of patients were scanned on the Premier, 21% on the Artist, and 17% on the Skyra. The mean TI for LV and RV signal suppression, respectively, were: 316.9 ± 63.2ms and 284.8 ± 53.3 ms (Artist), 334.4 ± 42.7 ms and 298.8 ± 36.8 ms (Premier), and 293.6 ± 30.2 ms and 255.7 ± 29.8 ms (Skyra). The TI needed to null the LV was significantly higher than the RV in all three scanners (p values: Artist =0.045, Premier < 0.0001, Skrya =0.0001). In the subgroup of HCM patients (n =7,mean age =57.71 ± 10y., 29% female), the LV wall thickness was 14.13 ± 2.81 mm with a mean TI of 329.71 ± 46.63 ms. The RV wall thickness was 4.37± 1.03 mm with mean TI of 298.86 ± 42.53 ms.

Conclusion:
This study found that the TI of the RV is lower than that of the LV, suggesting that evaluation of the RV muscle may require selection of TIs independent from LV TI selection.

27 - Endometriosis and Risk of Preeclampsia in Women Who Conceived Spontaneously: A Systematic Review and Meta-analysis

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Background:
We aimed to evaluate the association between endometriosis and the risk of preeclampsia and other maternal outcomes in spontaneously conceived women.

Method:
We systematically searched for articles on PubMed, MEDLINE, EMBASE, Scopus, Cochrane Library,Web of Science, and Google Scholar from inception until November 2021.

A total of 610 articles were reviewed once duplicates were removed. Inclusion criteria included spontaneous conception and surgical and/or imaging ascertainment of an endometriosis diagnosis. Exclusion criteria included conception using assisted reproductive technologies, multiple pregnancies, chronic hypertension, and unclear diagnoses of endometriosis. Data of selected studies were extracted, and analysis was performed on Review Manager,version 5.4. Quality assessment of included studies for potential risk of bias was evaluated using theNewcastle-Ottawa Scale (NOS) for cohort studies.

Results:
Three cohort studies of spontaneous pregnancies were included.Endometriosis was associated with an increased risk of preeclampsia (risk ratio [RR] = 1.47, 95% CI 1.13 -1.89, p = .003; I 2 = 0%; n = 3 studies). A sensitivity analysis excluding a study with adenomyosis cases yielded similar risk (RR = 1.44; 95% CI, 1.11-1.87; p = .006; I 2 = 0%; n = 2 studies). Having endometriosis did not significantly increase risk of cesarean delivery (RR = 1.38; 95% CI, 0.99-1.92; p = .06; I 2 = 80%; n = 2 studies) or postpartum hemorrhage (RR = 1.16; 95% CI, 0.46-2.91; p = .76; I 2 = 50%; n = 2 studies). According to NOS, the three cohort studies were attributed a high (7-8) score. This systematic review was considered heterogeneous in terms of clinical and statistical diversity.

Conclusion:
We detected an increased risk of preeclampsia in women with endometriosis who conceived spontaneously. Endometriosis did not seem to increase the risk of cesarean delivery and postpartum hemorrhage, but the number of studies was limited, and the heterogeneity was high.

53 - Differential Genetic Effects across Plasma Lp(a) Groups on Coronary Artery Disease

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Background:
Coronary Artery Disease (CAD) is the leading cause of death worldwide, thus presenting an extremely important direction for research into causal factors that may identify novel treatments. One such causal factor is plasma apolipoprotein a (Lp(a)), which is involved in the development of atherosclerosis and an independent risk factor for CAD. High plasma Lp(a) levels are a strong risk factor for CAD, but variable outcomes observed in people with high Lp(a) levels indicate there are other genetic factors at play. Genome-wide association studies (GWAS) have previously identified genetic variants associated with plasma Lp(a) levels. However, the mechanism of Lp(a)'s effect on CAD is still largely unknown. Performing GWAS on high-resolution next generation sequencing (NGS) data may help elucidate Lp(a)'s pathophysiological mechanisms.

Methods:
We conducted a GWAS in the UK Biobank split into two cohorts of subjects with either high or low plasma Lp(a) levels based on a threshold of 100 mg/dL. An additional GWAS analysis was conducted on all individuals with plasma Lp(a) as an interaction term for further filtering and confirmation. In addition, we examined UK Biobank whole exome sequencing (WES) data, allowing for the discovery of very rare variants likely to be involved in Lp(a)'s mechanism. After filtering, single nucleotide polymorphisms (SNPs) were ranked by their absolute difference in effect sizes between the high and low groups to identify variants with unique effects in high-LP(a) individuals.

Results:
Initial genotype analyses resulted in eight significant SNPs with large differential effects, within or near the genes SOX5, KIF2B, LINC02268, IGF2R, PTCH1, and ACTN2. Of particular interest was SOX5 OR(high Lp(a) p=7.32e-7, low Lp(a) p=5.36e-1), which has been associated with numerous cardiac parameters such as heart rate, atrial fibrillation, t-wave voltage, and PR interval. WES results indicated around 100 significant SNPs across plasma Lp(a) groups, including several rare variants with larger differential effect sizes. Among these findings is a SNP in the gene CESLR2 OR(high Lp(a) p=1.44e-1, low Lp(a) p=9.92e-7), whose proximity to the well-known gene SORT1 possibly indicates new mechanistic ties between SORT1 and Lp(a).

Conclusion:
The SNPs discovered in this differential GWAS and WES analysis as well as their respective genes may help uncover the biological mechanism of Lp(a)'s role in CAD, presenting possible targets for research into treatment.

26 - Automated Diagnosis of Pathological Heart Conditions Using Radiomic Features

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Background:
Medical imaging radiomics is an emerging field that uses processing techniques to extract quantitative features that characterize global and local photometric, geometrical, and textural properties of images. These objective features can be combined with machine learning techniques to automate assessment of disease. In this study, we aimed to evaluate the potential of radiomic features extracted from cardiac magnetic resonance images (CMR) for the classification of normal and pathological heart conditions. The pathologies include dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), and ischemic cardiomyopathy (ICMP).

Methods:
This study utilized the ACDC dataset consisting of 90 patients and 30 healthy controls to investigate the use of radiomic feature extraction for classifying normal and pathological heart conditions. Data analysis and algorithm development were carried out using the Python programming language. The volumetric stack of end-systolic cine short-axis images were used for feature extraction. Pyradiomics python package was used to compute 944 radiomic features from each stack. Due to class imbalance with a greater number of pathological cases than healthy controls, the SMOTE over-sampling methods was employed. Boruta feature selection was performed to identify 37 highly salient features. These were subsequently used to train a Random Forest classifier to distinguish between healthy and pathological heart conditions. The data was split into 80 cases for training and 40 cases for testing. Finally, a SHapley Additive exPlanations (SHAP) analysis was used to rank the salient features and explain their interactions with the predicted classes.

Results: We evaluated the model's performance using classification metrics and a receiver operating characteristic (ROC) curve on the testing dataset (30 with heart conditions (DCM, HCM, MINF) and 10 healthy cases). The model had an accuracy of 0.97, precision of 0.97, recall of 1.00, and F1-score of 0.98, indicating accurate classification of pathological heart conditions. The ROC curve had an area under the curve (AUC) score of 0.95. SHAP plots showed that Grey Level Non-Uniformity, sphericity, and coarseness were the most important features in predicting abnormal heart conditions. These features cannot be manually measured due to their complex nature and cannot be perceived by the human eye.

Conclusion: This study demonstrated that radiomic feature extraction on CMR cine images, combined with machine learning techniques, can be used to accurately classify normal and pathological heart conditions with high sensitivity, specificity and AUC. This method has the potential to efficiently and non-invasively stratify heart conditions in a clinical setting.

11 - Assessing the role of gender and social determinants of health on Coronary Microvascular Disease

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Background:
Patients presenting with typical cardiac chest pain, but no coronary artery disease were known to have cardiac syndrome X. Females are much more likely to have such syndrome, and more recently it was found that this presentation may be result of coronary microvascular disease which is typically not appreciated on cardiac catheterization. Most traditional risk factors for CAD are found to be significant for CMD as well. However, role of gendered social determinants of health remains to be determined. In this study we aim to elucidate traditional and social risk factors of patients with CMD.

Methods:
In this multicentre, case-control study, patients with chest pain syndrome and no coronary artery disease along with healthy volunteers were enrolled. Traditional cardiovascular including age, hypertension, diabetes mellitus, deslipidemia, and obesity, along with social determinant variables defined as income, education, employment status, anxiety, and depression were compared. GENESIS-PRAXY gender score was calculated for all subjects and compared amongst both groups. Composite traditional risk and social determinant risk scores were constructed to assess ranging from 0 (ideal) to 5 (worst) to assess the prevalence of each risk factor. Univariable, and multivariable logistic regression models were constructed to assess the risk of each variable for CMD.

Results:
Total of 104 (CMD N=55, mean age: 51.5±5.1, Control N= 49 mean age: 54.9±6.2) were enrolled in the study. Patients with CMD had a significantly higher prevalence of obesity (CMD: 11 (20%) vs Controls: 0(0%), P<0.001), type 2 diabetes mellitus (CMD: 12.7% vs Control: 0, P=0.01), and dyslipidemia (CMD: 45.5% vs Control: 0, P<0.001) compared to controls. Similarly, Social determinants of health risk factors also revealed that those in CMD group had significantly lower education level, and income, and were more unemployed and higher prevalence of depression with greater levels of anxiety. Gender score was significantly higher for CMD group compared to controls (CMD: 58.4±32.8 vs Control: 44.7±31.6, P=0.04). Multivariable model revealed TRF and social determinant risk factors to be significant predictors of CMD.

Conclusion:
Lower income, education, unemployment, depression and anxiety are some of the social determinants of health which have significant effect on CMD. Aside from such variables, traditional risk factors for CVD including hypertension, diabetes, dyslipidemia, and obesity are also important in patients with CMD.

45 - Frailty Screening At Scale Using Core Clinical Data And Supervised Machine Learning

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Background:
Frailty is a major risk factor for adverse health events in older adults with cardiovascular disease. We sought to develop and validate a predictive model leveraging clinical data available in the electronic health record to screen for frailty as defined by a prospective reference standard.

Methods:
We conducted a population-based cohort study using data from the Canadian Longitudinal Study of Aging (CLSA). From 2010-2015, the CLSA enlisted a diverse and multi-ethnic sample of community-dwelling adults 45-85 years of age. Comprehensive phenotyping was performed through interviews at participants' homes and assessments at data collection sites. Frailty was quantified by the 47-item Frailty Index (FI) Examination, consisting of tests for age-related deficits in physical performance, body composition, cardiopulmonary physiology, cognitive and sensory function. After dividing our sample into training (80%) and test (20%) sets, we compared machine learning models to predict the FI based on age, sex, diagnoses, and blood test results. We used the H2O AutoML platform (DAI 1.10.2) to determine the optimal model.

Results:
The cohort consisted of 30,097 adults with a mean age of 63 ± 10 years and 51% females. The mean FI score was 0.28 ± 0.08 (best to worst: 0.07-0.70). The light gradient boosted model (LGBM) had the highest accuracy with a 4.54% mean average error to predict the FI-Exam score. The final LGBM model selected 22 features in descending order of relative importance (1.00-0.003): age, cardiac disease, hypertension, elevated high-sensitivity C-reactive protein, glycated hemoglobin, low high-density lipoprotein, male sex, elevated red cell distribution width, diabetes, low vitamin D levels, elevated white blood cell count, peripheral artery disease, COPD, glaucoma, memory impairment, cataracts, elevated creatinine, elevated total cholesterol, pneumonia, elevated MCV, stroke and urinary incontinence.

Conclusion:
Frailty screening can be performed at scale for clinical or research purposes using common clinical and biochemical inputs. Our machine learning model predicted frailty with high accuracy and a manageable number of inputs, yielding pathophysiological insights about their relative importance.

7 - Decoding Calcific Mitral Valve Disease: a novel deep learning model uncovers the role of calcium burden - *Abstract Retracted*

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Background:
Mitral annular calcification (MAC) is a common degenerative disease that affects older adults and causes calcium deposition in the mitral annulus, increasing the risk of mitral valve (MV) dysfunction, cardiovascular events, conduction abnormalities, and mortality. While the primary imaging modality recommended for the clinical evaluation of MAC is echocardiography, MAC is found incidentally in 8% of routine thoracic computed tomography (CT) scans. CT scan is a sensitive imaging modality for assessing MAC, providing the resolution necessary to understand the anatomical involvement of calcification. The exact correlation between the CT calcium burden and the degree of severity of mitral valve disease is unclear.

Purpose:
Our study aimed to determine the association between MAC, as assessed on CT, and significant mitral stenosis (MS) or mitral regurgitation (MR), as visualised on echocardiography. In addition, we sought to determine the quantitative MAC cut-offs that would optimally predict significant MS or MR on echocardiography.

Methods:
A retrospective cohort study was conducted at Jewish General Hospital. Inclusion criteria were: age≥60 years, resting transthoracic echocardiogram performed between 2013-2022, non-gated chest CT performed within one year before echocardiography for clinical indications unrelated to MV disease, and any degree of MAC documented on the echocardiography report. Exclusion criteria were: prior MV intervention, endocarditis, and congenital MV disease. Significant calcific mitral valve disease (CMVD) was defined as ≥moderate MR and ≥mild MS on the echocardiography report, ascertained by expert readers based on multiparametric ASE criteria. MAC volume was quantified on the multi-slice CT DICOM images using a 3D U-Net deep neural network previously trained by our group on an independent cohort.

Results:
The cohort consisted of 1,560 unique patients with a mean age of 79 and 61% females. The echocardiographic prevalence of significant MR and MS was 10% and 4%, respectively, for 211 affected patients. The CT-based mean MAC volume was 949 mm^3 in patients with significant MR or MS, as opposed to 334 mm^3 in those without (P<0.001). MAC volume >1000 mm^3 was the optimal cut-off to predict significant MS (specificity 90%, sensitivity 51%, area under ROC curve 0.79) and significant MR (specificity 89%, sensitivity 21%, area under ROC curve 0.60). Adjusting for age, sex, and comorbid conditions did not affect the observed association between MAC volume and mitral valvulopathy.

Conclusion:
A novel deep-learning model for quantifying MAC volume from non-cardiac CT scans efficiently screened for CMVD, particularly MS, and identified patients who may benefit from further evaluation.

44 - Plasma proteomic biomarkers of aortic stenosis: a mendelian randomization study

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Background:
Plasma proteomic analysis has become more feasible since large-scale measurements have been developed to analyze up to 7,000 proteins simultaneously. Multiple studies have already adapted these methods to generate protein expression profiles of plasma samples. With the integration of genomic and proteomic data, large-scale protein quantitative trait loci (pQTL) studies have successfully identified several pQTLs related to diseases and medical phenotypes. In addition, combining Mendelian randomization (MR) and pQTLs has demonstrated its usefulness for identifying causal contributors to diseases.

Methods:
Two sample Mendelian randomization was used to identify causal contributors to aortic stenosis in human plasma proteins. Publicly available pQTL results (deCODE and ARIC) were analyzed with a meta-analysis of nine aortic stenosis (AS) GWAS (Meta-AS). We evaluated the results using several methods, including MR-egger, bidirectional MR, and colocalization. AS GWAS results from the Million Veteran Program (MVP) were used as a replication study. In addition, MR analysis for coronary artery disease (CAD) using UK biobank GWAS results was conducted to explore the differences in plasma markers between AS and CAD.

Results:
We obtained 1,706 pQTLs with 5,533 independent variants from deCODE summary statistics. The Meta-AS containing 13,347,173 associations, was the outcome of the MR analysis. After harmonizing the genetic variants between the pQTLs and Meta-AS, MR analysis was conducted using 1,563 pQTLs. With an FDR of <0.05 in the discovery phase, using deCODE pQTLs, we identified three candidate proteins (PLG, COMP, and COL2A1) and five potential proteins (PLG, ACE, G3BP1, ATOX1, and SELM) using the ARIC cis-pQTLs. Only PLG was significant in both the deCODE and ARIC pQTL datasets ($p = 4.07 \times 10^{-5}$, $p=8.97 \times 10^{-6}$ respectively). In the replication study using MVP, PLG was also the most significant finding ($p = 3.13 \times 10^{-9}$).

To address the pathophysiological processes that are common between AS and CAD, we also conducted an MR study using CAD GWAS results from the UK biobank and the two sources of pQTLs. Six proteins (PCSK9, LY75, CTRB2, HGFAC, ITIH3, and IL6R) passed the corrected p-value threshold and sensitivity tests.

Conclusion:
We performed a pQTL MR analysis for AS and CAD. The most consistent candidate for AS is PLG, located near the *LPA* gene. Additional research in larger studies using pQTLs as intermediate phenotypes will identify more causal factors for both AS and CAD.

20 - Efficacy of CardioMEMS on decreasing heart failure hospitalisation rate: HTA report

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Background:
Elevated pulmonary artery pressure (PAP) occurs days or weeks before clinical congestion. CardioMEMS is an implantable sensor system use for monitoring PAP to guide heart failure management. PAP data are used by doctors to adjust treatment accordingly. Currently, CardioMEMS is not available at the MUHC. This review assessed the evidence on the effectiveness of CardioMEMS to reduce heart failure hospitalisations compared to standard care in heart failure management.

Method:
A systematic search was conducted in 4 databases of all relevant articles evaluating the association between CardioMEMS and heart failure hospitalisations in New York Heart Association (NYHA) class III patients. Data extraction and quality assessment was performed on the studies included in the report. Findings were summarised in a narrative synthesis. Cost impact analysis of CardioMEMS at the MUHC vs standard care management was also done.

Results:
Two randomised controlled trials (RCT) and 10 non-randomised studies were included in our review. Five of the 10 non-randomised studies were related to 1 RCT, either as a subgroup analysis or follow-up study. For NYHA class III patients, 1 RCT (HR=0.63, 95% CI: 0.52-0.77, n=550) and all 10 non-randomised studies reported a lower risk of heart failure (HF) hospitalisation in patients monitored with CardioMEMS compared to patients managed with standard care. However, these studies were at high risk of bias. Conversely, for NYHA class II-IV patients, the risk of HF hospitalisation did not differ significantly between CardioMEMS and standard care in HF management (HR=0.83, 95%CI: 0.69-1.01, n=1000). The cost of HF management with CardioMEMS was estimated to be $14,734 ($13,055 - $17,006) more expensive than standard care management for each NYHA class III patient.

Conclusion:
Low quality evidence suggests that CardioMEMS may reduced heart failure hospitalisations in NYHA class III patients. However, there is a high uncertainty about the results given the poor-quality evidence. Consequently, CardioMEMS was not recommended due to inadequate evidence and high cost.

8 - Electrocautery-induced Inappropriate Implantable Cardiac Defibrillator Shock

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Background:
Inappropriate Implantable Cardiac Defibrillator (ICD) shock due to electromagnetic interference (EMI) induced by electrocautery is a well-known theoretical association but is rarely reported. We report a case of EMI induced by electrocautery causing inappropriate ICD shock.

Case:
A 72-year-old patient underwent surgery because of left inguinal hernia. He had a history of myocardial infarction, hypertension, diabetes mellitus, chronic obstructive lung disease, paroxysmal atrial fibrillation with left bundle branch block, left ventricular ejection fraction of 25%. Three years earlier the patient underwent implantation of cardiac resynchronization therapy (CRT-D). On the day of surgery, the patient was placed in supine position and the electro dispersive pad (EDP) on his left flank. During the operation with the use of monopolar electrocautery the CRT-D defibrillated. The surgical procedure was paused and a magnet was placed on the CRT-D. Then the procedure was completed with no complications. A subsequent CRT-D interrogation confirmed its normal functioning and inappropriate intraoperative 30 joule shock due to EMI.

Discussion:
Many patients with ICD undergo surgical procedures that use electrocautery, particularly monopolar devices, that require a dispersive electrode (EDP) applied to the patient's skin to complete the electrical circuit. It has been recommended that the EDP should be positioned to direct its returned current away from the pulse generator and lead in order to reduce the risk of EMI. Guidelines regarding ICD management during surgery inferior to the umbilicus are not very clear. Using monopolar devices, for cardiac and non-cardiac surgery superior to umbilicus, a high occurrence of EMI has been reported, despite different placement of EDP. Therefore, it has been advised that the cardiac implantable electronic device should be altered to an asynchronized pacing mode in the pacing dependent patient and that ICD's antitachycardia function should be temporarily suspended. On the contrary it has been reported that the risk of EMI does not occur in any lower abdominal or extremity procedures, implying that suspending antitachycardia therapy is likely unnecessary in these patients. Our patient underwent surgery under the umbilicus and the EPD was positioned in the left flank. The EPD returned current might have interfered with the CRT-D and caused EMI. Guidelines regarding EDP placement are lacking and are based only on expert consensus or isolated case reports.

Conclusion:
Our case underlines that with the use of monopolar cautery not only the location of the surgery but also EDP placement may be important in order to avoid EMI.

14 - Association Between Maternal Hypertension and Infant Neurodevelopmental Outcomes in Extremely Preterm Infants

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[1]McGill

Background:
Maternal hypertension is associated with prematurity and its complications in neonates, but it is unclear whether preterm infants exposed to maternal hypertension experience poorer neurodevelopmental outcomes compared to infants born prematurely without exposure to maternal hypertension.

Objectives:
We aimed to assess the association between exposure to maternal hypertension and neurodevelopmental impairment (NDI) at 24 months of age, compared with no such exposure in a cohort of extremely premature infants born < 29 weeks of age.

Method:
This retrospective study used data from two neonatal units and included infants born between 23^{+0} and 28^{+6} weeks from 2011 to 2017. Exposure was the presence of maternal hypertension with/without being born SGA. Outcomes were the presence of any or significant NDI; each was a composite, including elements derived from Bayley Scales of Infant and Toddler Development, third edition. Logistic regression models assessed associations between maternal hypertension with/without SGA and NDI, adjusted for diabetes, gestational age, cesarean delivery, or premature rupture of membranes.

Results:
Of 1019 preterm infants, we included 647 infants (median gestational age 26 weeks, IQR: 25-28), 96 (15%) were exposed to maternal hypertension, 71 of these (11% overall) were exposed to maternal hypertension and were SGA status, 551 (85%) were unexposed to maternal hypertension, and 28 of these (4% overall) were unexposed to maternal hypertension but were SGA. Infants exposed to maternal hypertension had higher rates of any NDI (n=55/96 (57%) vs. n=252/551 (46%)) and significant NDI (n=21/96 (22%) vs n=86/551 (16%)). Maternal hypertension was associated with any NDI (OR: 1.64; 95%CI=1.06-2.55), and significant NDI (OR: 1.51; 95%CI=0.87-2.55) at 24 months. Maternal hypertension with SGA was associated with any NDI (OR: 3.23; 95%CI=1.38-8.42) and significant NDI (OR: 3.80; 95%CI=1.60-8.69). After stratification by gestational age category (< 26 weeks and ≥26 weeks), infants exposed to maternal hypertension born ≥ 26 weeks (traditionally less at risk of NDI) still showed significantly higher odds of any NDI (1.9; 95% CI= [1.18-3.09]).

Conclusion:
Maternal hypertension was associated with a higher risk of NDI in extremely preterm infants, particularly with SGA.

48 - MixEHR-SURG: A semi-supervised multi-modal survival topic model for automatic phenotyping using the electronic health record

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[1]McGill

Background:
Electronic Health Records (EHRs) contain heterogeneous personal clinical data, and their widespread adoption has resulted in large-scale EHR databases. Machine learning techniques, including topic models, have been developed using EHR to identify phenotypic correlations and predict patients' disease risks. Existing topic modeling methods are often hindered by a lack of reliable disease labels for interpreting topics and a failure to incorporate predictive properties and survival-associated information. To address these limitations, we propose a modified MixEHR model that aims to enhance the interpretability and predictiveness of the model.

Method:
The MixEHR model is a topic modeling technique that uses EHRs to identify phenotypic correlations. We propose a modified MixEHR model that includes survival information supervision to facilitate survival-supervised disease topic learning. Our model allows for the prediction of patient survival curves and identification of EHR feature clusters associated with survival outcomes. The generative process begins with mapping ICD codes to phenotype codes for Phenome-Wide Association studies (PheWas) and obtaining a phenotype code frequency table. The frequency table and token list frequency hyperparameters are used to generate clinical features and survival information. We estimate model parameters using modified stochastic collapsed variational inference to account for complex variable dependencies.

Results:
We evaluated the interpretability and prediction accuracy of our model using simulation and applied it to two real EHR datasets. The first dataset was the Quebec congenital heart disease (CHD) database, which includes 84,498 patients and 28 years of follow-up from 1983 to 2010. We used all EHRs before a patient's first heart failure discharge to predict their death time. The second dataset was the MIMIC-III relational database, which contains data from 38,597 adult patients and 7,870 neonates admitted to critical care units between 2001 and 2012. We incorporated a patient's EHRs during their first inpatient period to predict their mortality time. We compared our model with the baseline MixEHR method and evaluated the predictive results using the concordance index and dynamic cumulative area under the receiver operating characteristic (ROC) curve. Our model achieved precise survival information predictive properties with more interpretable and clinically meaningful topics.

Conclusion:
Our model improves topic modeling techniques by incorporating survival information supervision and trustworthy phenotypes as topic priors, resulting in increased interpretability and predictiveness. We applied this model to two real EHR datasets and achieved more precise survival information predictive properties with clinically meaningful topics.

28 - A sex-stratified analysis of gendered social determinants of health and adverse cardiovascular outcomes in atrial fibrillation

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Background:
Atrial fibrillation (AF) is the most common arrhythmia and is associated with a higher risk of major adverse cardiovascular events (MACE) and all-cause mortality. However, models addressing adverse outcomes have not been conducted separately in males and females, nor have they included social determinants of health (SDOH), which are known to be strong predictors of cardiovascular (CV) outcomes. Additionally, SDOH have been shown to be gendered, meaning that they are unevenly distributed between females and males and may impact females and males with AF differently. The aim of this study was to develop sex-stratified predictive models to identify sex differences in the associations between gendered SDOH and adverse outcomes in patients with AF.

Method:
The study population was drawn from the European Society of Cardiology-European Heart Rhythm Association EURObservational Research Programme-Atrial Fibrillation (ESC-EHRA EORP-AF) General Long-Term Registry. In addition to the CHA_2DS_2-VASc variables, gendered SDOH were included: education, living alone vs. not, gender inequality index (GII) (a measure of sex inequity at the country level), and the subscales of the EQ-5D-5L questionnaire. The study outcome was a composite of major adverse cardiovascular events (MACE: ACS, stroke/transient ischemic attack/thromboembolism, and CV mortality) and all-cause death. Sex-stratified logistic regressions were performed.

Results:
The study population comprised 11,096 patients (mean age 69.2 years; 40.7% females) living in 27 European countries. Females with AF smoked less, consumed less alcohol, reported lower quality of life, and had poorer health than men. They were also more likely to live alone, have lower levels of education, engage less in regular physical activity, and have higher levels of anxiety. In sex-stratified analyses, fewer SDOH associations were observed with the composite outcome in the female model than in the male model. In females, only regular exercise was associated with the outcome (OR: 0.61; 95% CI: 0.41-0.88). In males, moderate difficulty with self-care (OR: 1.59; 95% CI: 1.25-2.05) and smoking (OR: 1.24; 95% CI: 1.07-1.44) were associated with a higher risk of MACE and all-cause mortality, while higher self-reported health (OR: 0.96; 95% CI: 0.92-0.99) and regular exercise (OR: 0.77; 95% CI: 0.64-0.92) were associated with a lower risk of the same outcome.

Conclusion:
Different gendered SDOH are associated with the risk of MACE and all-cause mortality in European females and males with AF. Addressing specific social determinants of health for women and men separately may improve outcomes in patients with AF.