Schulich School of Medicine & Dentistry

Western University

Department of Medicine

RESEARCH DAY

Friday, May 20, 2022

Virtual Event

This program has no commercial support.

CME INFORMATION

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by Continuing Professional Development, Schulich School of Medicine & Dentistry, Western University. You may claim a maximum of 5.0 hours (credits are automatically calculated).

Each participant should claim only those hours of credit that he/she actually spent participating in the educational program.

25% of this program is dedicated to participant interaction.

Scan the QR code to complete the **Participant Evaluation** form online:

By the end of this research day, participants will be able to:

- describe new research findings of relevance to Internal Medicine and related subspecialties.
- recognize clinical research conducted by the trainees in the Department of Medicine.
- identify basic research conducted by trainees in the Department of Medicine.

Dr. Straus Learning Objectives:

1. To define knowledge translation, including end of grant and integrated knowledge translation.
2. To describe how to develop a knowledge translation plan.

Dr. Chandy Learning Objectives:

1. To explain the cardiovascular effects of marijuana use.
2. To explain how genistein blocks the adverse effects of marijuana.

Dr. Leligdowicz Learning Objectives:

1. To review how heterogeneity among critically ill patients complicates treatment decisions and outcomes.
2. To describe novel translational biology tools that can improve our understanding of complex syndromes.

Brief Biosketches for Keynote and Faulty Speakers

Keynote Speaker:

Dr. Straus MD, FRCPC, MSc

Sharon E. Straus is a geriatrician and clinical epidemiologist who trained at the University of Toronto and the University of Oxford. She is the Director of the Knowledge Translation Program and Physician-in-Chief, St. Michael's Hospital and Professor in Department of Medicine, University of Toronto. She holds a Tier 1 Canada Research Chair in Knowledge Translation and Quality of Care and has authored more than 500 peer-reviewed publications and 3 textbooks in evidence-based medicine, knowledge translation and mentorship. Since 2015, she has consistently been in the top 1% of highly cited clinical researchers as per Clavirate and has an H-index of 106. She holds more than $60 million in peer-reviewed research grants as a principal investigator. She has received national awards for mentorship, research and education. She was inducted as a Fellow in the Royal Society of Canada in November 2021 and named as a Member of the Order of Canada in December 2021

Faculty Speakers:

Dr. Chandy MD, PhD, FRCPC:

Dr. Chandy completed his MD/Ph.D. at Pennsylvania State University. His doctoral thesis was chromatin dynamics with Dr. Jerry Workman. After completing medical school, Dr. Chandy trained in Internal Medicine at the University of British Columbia, followed by a Cardiology fellowship at the University of Toronto. Dr. Chandy also completed a fellowship in Echocardiography and enrolled in the Clinician Scientist Training Program at the University of Toronto under the supervision of Dr. Mansoor Husain. Dr. Chandy used his training in biochemistry, chromatin remodeling, and cell culture to study vascular biology using small animal models. With a desire to learn more about stem cell biology, Dr. Chandy trained in the laboratory of Dr. Joseph Wu, a world-renowned expert in stem cell biology and the Director of the Stanford Cardiovascular Institute. Here, Dr. Chandy learned how to reprogram human induced pluripotent stem cells (hiPSCs). Human iPSCs provide a limitless tissue supply with an individual's unique genetic code for personalized disease modeling, drug discovery, and regenerative medicine. Dr. Chandy also learned how to design experiments to leverage iPSC disease modeling and understand the mechanisms of cardiovascular disease. Dr. Chandy's current research focuses on understanding the pathophysiology of environmental exposures such as air pollution, e-cigarettes, and marijuana on cardiovascular disease using human iPSC-derived tissue. Dr. Chandy's laboratory employs next-generation sequencing (NGS), proteomics, and gene editing to decipher the mechanisms of cardiovascular disease.

Dr. Leligdowicz MD, DPhil, FRCPC:

Dr. Leligdowicz is a clinician scientist in the Department of Medicine in the division of Critical Care Medicine. She completed a medical degree at McGill University and a PhD at Oxford University in human HIV immunology in West Africa. Following residencies in internal medicine (UBC) and adult critical care (UofT), she pursued her interest in immunology and severe infection as a postdoctoral research scholar at UCSF. Her laboratory at Robarts Research Institute uses cellular and molecular tools to study prospective biological samples from patients admitted to the Intensive Care Unit (ICU) to understand the mechanisms of immune regulation in severe infection. The focus of her research is translational biology of immune responses and endothelial injury in early sepsis, to understand pathology, improve diagnosis, and personalize treatment of this complex syndrome.

AGENDA

DoM Resident Research Day 2022
Friday, May 20, 2022

Moderators Drs. Richard Kim and Reena Khanna

Start	End	Schedule of Events
8:30	8:40	Welcome & Opening Remarks Dr. Richard Kim
8:40	9:30	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
9:30	9:55	Faculty Presentation - Dr. Mark Chandy “Cannabinoid Receptor 1 Antagonist Genistein Attenuates Marijuana-Induced Vascular Dysfunction” 20 min presentation, 5 min Q&A
9:55	10:10	BREAK (15 min)
10:10	11:00	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
11:00	11:50	Keynote – Dr. Sharon Straus “Knowledge translation - what it is and what it isn't” 40 min presentation, 10 min Q&A
11:50	12:50	LUNCH BREAK (60 minutes)
12:50	1:15	Faculty Presentation - Dr. Aleks Leligdowicz “Deconvoluting complex clinical syndromes: From bed to benchside” 20 min presentation, 5 min Q&A
1:15	2:05	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
2:05	2:20	BREAK (15 min)
2:20	3:00	Trainee Oral Presentations 4 presenters 7 min presentations, 3 min Q&A
3:00	3:15	Closing Remarks Dr. Richard Kim

Trainee Oral Presentations

Time		Presenter	Level	Title	Pg
8:40	8:50	Little, Derek	Clinical Fellow	Effectiveness of Balloon-occluded Retrograde Transvenous Obliteration for Primary Prophylaxis of Gastric Variceal Bleeding: A Systematic Review	31
8:50	9:00	YusufIbrahim, Aisha	PGY-4	Joint pain and functional impairment in patient with acromegaly.	56
9:00	9:10	Hillyer, Alexandra	MD Student	COVID-19 Vaccine Humoral Response and Treatment Effect in Patients with Hematologic Malignancy	24
9:10	9:20	Manji, Aminmohamed (Amin)	PhD Student	The role of aging on microvascular endothelial barrier function within the lungs	34
9:20	9:30	Ghassemian, Artin	PGY-4	Reducing pleural fluid flow cytometry testing - shared decision making between the clinic and laboratory	19
10:10	10:20	Chaudhary, Rushil & Jordan Ho	PGY-3	Development of a convolutional neural network to identify pleural effusion on lung ultrasound: a deep learning study	15
10:20	10:30	Graham, Emma	MSc Student	E-cigarette vapour impairs pulmonary surfactant	20
10:30	10:40	To, Eric	PGY-4	Quality Improvement Initiative to Optimize the Care of Patients with Sickle Cell Disease Presenting to the Emergency Department with Vaso-Occlusive Pain Crisis	48
10:40	10:50	Larsen, Frederikke	PhD Student	DNA Hypomethylation Inhibits Tuft Cell-Derived Colitis-Associated Cancer	30
10:50	11:00	Parker, Brent	PGY-4	Effect of Levofloxacin Prophylaxis on Rates of Febrile Neutropenia in Patients Receiving DA-EPOCH-R Chemotherapy for Aggressive Lymphomas	40
1:15	1:25	Tong, Jeffery	PGY-4	Improving the efficiency of virtual insulin teaching for patients admitted to hospital through the COVID-19 pandemic	48
1:25	1:35	Winger, Kathleen	PGY-3	Pragmatic Evaluation of an Algorithm using D-dimer Adjusted to Clinical Probability in the Diagnosis of Pulmonary Embolism	53
1:35	3:10	Hindi, Zaid	PGY-5	Incidence and Predictors of Non-Hepatic Cancers in Alcohol Related Liver Disease in the WALDO Cohort	25
1:45	1:55	Martin Calderon, Leonardo	PGY-2	HIGHER RESOURCE UTILIZATION IN PATIENTS WITH SYSTEMIC SCLEROSIS COMPLICATED BY DIGITAL ULCERS	36

1:55	2:05	Madrazo, Lorenzo	PGY-3	"It's what we can do for now"□: Professional Identity Formation Among Internal Medicine Residents During the COVID-19 Pandemic	33

2:20	2:30	Tauqir, Maria	PGY-2	The Association between Vedolizumab and the Development of New-Onset Features of Spondyloarthritis in Patients with Inflammatory Bowel Disease: A Pilot Study.	46
2:30	2:40	Garapick, Reidun	MD Student	Paramedics' ability to determine diagnosis and most appropriate destination in patients who activate 9-1-1.	18
2:40	2:50	Wang, DongYao (Donald)	PGY-2	The role of CUB And Sushi Multiple Domains polymorphism as a genetic predictor of aromatase inhibitor induced arthralgia in post menopausal estrogen receptor positive breast cancer patients	52
2:50	3:00	Adeusi, Lade	PGY-2	"Newest Kid in Town": Apo B versus LDL cholesterol levels - are they interchangeable?	8

POSTER presentations

- Trainee Poster presentations for judging will run simultaneously with Trainee Oral presentations
- Drop-in poster viewing will be available between 8:30 a.m. and 3:00 p.m.
- Poster presenters will be available between 12:20 p.m. and 12:50 p.m. to answer your questions and discuss their poster
- Poster viewing is available here: https://uwoclinpharm.lawsonresearch.ca/poem/research_day/rd_posters.php

List of All Submitted Abstracts (in alpha order)

Lade Adeusi

"Newest Kid in Town": Apo B versus LDL cholesterol levels - are they interchangeable?

Olivia Zhu, Murray W. Huff and Robert A. Hegele

Background: Clinical practice guidelines focus on low-density lipoprotein cholesterol (LDL-C) to guide healthcare providers and patients. However, LDL-C has several limitations. In 2021, the Canadian Cardiovascular Society dyslipidemia guidelines recommended alternate treatment thresholds using apolipoprotein (apo) B, the protein component of LDL particles. Specifically, the recommended thresholds to intensify statin therapy are now LDL-C >1.8 mmol/L and apo B >0.7 g/L, variables that are considered as interchangeable. Methods: To evaluate the real-world correlation between LDL-C and apo B, we reviewed records of 728 patients (41.8% females, age 49.3+18.5 years) from LHSC University Hospital Lipid Clinic. We excluded patients with TG >5 mmol/L because of interference with LDL-C determination. Results: Mean + SD LDL-C and apo B were 2.92+1.09 mmol/L and 1.01+0.28 g/L, respectively. Overall, R2 between LDL-C and apo B was 0.758 (P<0.0001). 8.68% of individuals had LDL-C <1.8 mmol/L and apo B >0.7 g/L, while 1.85% of individuals had LDL-C >1.8 mmol/L and apo B <0.7 g/L. Thus, while LDL-C and apo B are generally well correlated, almost no subject who attained the apo B threshold remained above their LDL-C threshold, while substantially more subjects who attained the LDL-C threshold remained above the apo B threshold. Conclusions: LDL-C and apo B levels are closely but incompletely correlated. Attaining the apo B threshold <0.7 g/L ensures that almost all patients concurrently attain the LDL-C threshold <1.8 mmol/L. If guideline-based clinical decision-making was to focus on only one variable, apo B would seem to be preferable over LDL-C.

Qasem Alkhateeb

Prevalence of chronic conditions in Syrian refugees to Ottawa: The cases of Hepatitis B and C

Dolly Lin, Olivia Magwood, Rebecca Warmington, Laura Muldoon, Qasem Alkhateeb and Kevin Pottie

Background: Forcibly displaced migrants, such as refugees, often experience disruptions to their healthcare during their migration journey. Resettlement countries require evidence on disease burden to inform their preparedness for linkage and care. The objective of this study was to explore the prevalence of multiple chronic conditions,

including Hepatitis B (HBV) and C (HCV) infections among resettled Syrian refugees to Ottawa, Ontario.Methods: This was a cross-sectional study in 4 primary healthcare clinics in Ottawa during the first wave of Syrian refugee arrival (December 2015- April 2016). We reviewed the medical charts of patients identified as Syrian refugees for evidence of chronic condition diagnosis, two of which were Hepatitis B (ascertained with surface antigen tests) and Hepatitis C (with antibody tests) infections. We used descriptive statistics to calculate the prevalence of these conditions, and Chi2 or Fisher Exact tests to explore sex differences.Results: A total of n=582 participants were screened for HBV with a prevalence of 0.9% (0.0-2.0), and n=612 were screened for HCV with a prevalence of 0.7% (0.0-1.4%). No cases occurred in the same family and any differences between sexes were not statistically significant for HBV nor HCV (p=.12 and .19, respectively). Discussion: The prevalence of HBV and HCV infections among Syrian refugees were comparable to that of Canadian-borns. This highlights the need to follow existing Canadian practices, such as screening pregnant women and those with high-risk behaviors, among this population

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Aiman ALWahaibi

FLUID PRIME - Effect of lactated Ringers compared to saline on acute kidney injury: a sub-study of FLUID

Dr. Claudio MartinDr. Lauralyn McIntyre

Administration of IVF to the admitted patients is the most common procedure which my significantly influence their outcomes. The current literature revealed a gap which needs large studies to overcome that. Also, due to different challenges of designing good trials to provide high quality data as many studies use a variety of clinical outcomes measures such as mortality and morbidity which make the comparison difficult. Based on latest systematic review there was no mortality difference between RL and NS in critically ill patients which has high certainty of evidence, but the effect on preventing acute kidney injury was similar with low certainty of evidence. This study will use approach of a multi-center randomized, cluster cross-over controlled clinical trial testing superiority of LR compared to NS in patients receiving IV fluid as resuscitation fluid in hospital. The primary goal to determine if normal saline induces acute kidney injury or worsens chronic kidney disease in comparison to Ringers lactate in hospitalized patients. More importantly, the results of this study will have the power to improve patient's quality of recovery following IV fluid administration to all admitted patients. All admitted patients will be recruited, and randomized to receive one of two IV solutions for 2 periods, each period will last for 3 months. At the end will check the primary end points. Also, will look to secondary end points: electrolytes, use of vasoactive medication infusion , hospital mortality, length of stay as admission and ICU length of stay will be addressed.

Monica Arnaldi

Podocalyxin (PODXL) nonsense variant as a candidate gene associated with Focal and Segmental Glomerulosclerosis (FSGS).

Dervla M. Connaughton

Introduction Rare kidney disease has been the focus of many investigative efforts, among the podocyte proteins, the PODXL-encoded podocalyxin as a member of the CD34 family of stem cell sialomucins, has been recently associated with both recessive (compound heterozygous variants) and dominant forms of familial nephropathies (OMIM Entry * 602632). Through familial exome sequencing, three affected individuals belonging to a family with Focal Segmental Glomerulosclerosis (FSGS) revealed a novel variant in a highly attractive candidate gene, a heterozygous nonsense variant in the PODXL gene c.1048C>T, p.(Arg350*).FSGS, a podocyte-driven disease, is the most frequent diagnosis of kidney disease worldwide, and regularly progresses to end-stage renal disease (ESRD).DiscussionIn the past decade, genetic testing has shown a significant advance, the most frequently used technique for genetic testing is a next-generation sequencing (NGS). PODXL gene has been reported to the gnomAD population database with a minor allele frequency (MAF) of 0.003% (1/30932 alleles). Cases in the literature, although limited, do share a similar phenotype with the onset of proteinuria and biopsy findings, showing FSGS. Here we show a family carrying a similar heterozygous nonsense mutation in the PODXL gene and FSGS disease.ConclusionA variant form of PODXL remains the most likely candidate causing FSGS in families with autosomal dominant inheritance. The use of NGS is expected to increase diagnostic efficiency for rare kidney diseases. A definite genetic diagnosis could have important prognostic value, and the adequate delivery and integration of genetic information should be implemented.

Liana Balaghi

An Increase in Atypical Presentations of Giant Cell Arteritis with Large Vessel Involvement at St. Joseph's Health Care London: A Case Series

Lillian Barra

Giant cell arteritis (GCA) is a vasculitis involving medium and large arteries in individuals > age 50. Involvement of aortic cranial branches results in the classical symptoms, including headache, jaw claudication, scalp tenderness, and vision change. Extracranial large vessel (LV) involvement is seen in 15-20% of cases, and can lead to limb artery stenosis, aortic dissection and aneurysm. LV-GCA presenting with primarily constitutional symptoms is uncommon, posing a diagnostic challenge as other differentials, such as infection or malignancy need to be ruled out. This series describes atypical presentations of GCA in patients with LV abnormalities on imaging. Four females and one male (aged 62-72) referred to a rheumatologist between April and

September 2021 at St. Joseph's Health Care London were included. Three patients presented with fevers, one with night sweats and one with weight loss. Two had headaches (intermittent, mild, and resolved spontaneously) and two had non-specific ocular symptoms without vision loss. All patients had vessel wall thickening and/or enhancement, or artery stenosis on CTA or PET scans. Four patients underwent temporal artery biopsy (TAB), three of which were diagnostic of GCA. All patients had elevated inflammatory markers, with mean ESR 79.6 mm/hr and CRP 138 mg/dL. TAB can be helpful for diagnosing LV-GCA in patients with constitutional symptoms. The number of referrals for LV-GCA has increased in the last year. Whether this is related to increased awareness of GCA, improved ability to pick up LV involvement on imaging, or a higher incidence of LV-GCA in the region is unclear.

Alexandra Basden

Reducing readmissions of general medicine patients admitted at Victoria Hospital by enhancing patients' capacity for self-care: A quality improvement intervention

Alexandra Basden

Background:As per the Canadian Institute for Health Information, in the year 2020 1 in 11 patients were readmitted within 1 month of discharge from hospital in Canada resulting in a 30 day readmission rate of 9.4%, with the Ontario RA of 9.6%. As a result, Readmission to hospital in Canada cost more than 2.3 billion dollars yearly. A systematic review of previous study interventions aimed at reducing readmissions concluded that most interventions generated mixed results, had observational design, significant heterogeneity and were tested on specific patient populations making their findings challenging to generalize to general medicine patients.Aim: To decrease readmission rate of patients admitted to VH CTU Blue team by 30 % in 1 year Methods:This study implemented a PDSA method aiming to test a patient-centered intervention to enhance patient's capacity for self-care for safer transition to home by utilizing a Transitional Coach, who delivered a standardized comprehensive patient education, discharge planning and follow-up using a checklist. These PDSA cycles were carried out in 3 distinct phases, firstly providing patient information to all individuals meeting inclusion criteria, the second and third to provide telephone and when needed in person follow-up to high risk patients as identified by a LACE score >10. Additionally, we collected 30 day readmission data to further expose the most prevalent reasons for readmission locally at LHSC. Results:Measured baseline rate of readmission is approximately 28%, reduced to 14% in phase 1 and 20% in phase 2.

Amy Basilious

Current practice patterns in intensive care units for the prevention of exposure keratitis

Mary Feng, Leah Nicoletti, Rookaya Mather

Purpose: To assess practice patterns in intensive care units (ICUs) for the prevention of exposure keratitis. We report three cases and present evidence-based recommendations for ocular care protocols.Methods: Twenty-four ICUs in Ontario were surveyed by telephone. Questions focused on eyelid closure assessment, eye care protocols, methods of ocular surface protection, identification of complications, and criteria for ophthalmology consultation.Results: Responses were collected from 18 ICUs, with 5 (28%) reporting an eye care protocol for unconscious patients. While 13 (72%) reported a protocol for patients unable to close their eyes, eyelid closure was only formally assessed in 10 (56%) ICUs. Ointment and artificial tears were common components of eye care protocols, with 15 (83%) using both. Most protocols indicated the use of lubricant drops or ointment on an as needed basis. The main reasons for ophthalmology consultation were infection and redness. Corneal complications such as abrasions and ulceration were the most recent ocular complications encountered.Conclusion: Practices to prevent exposure keratitis vary across ICUs, with some having no standard protocols in place for ocular protection. We propose universal precautions on admission to ICU for all unconscious patients or patients who cannot blink or close their eyelids. An evidence-based protocol would involve instillation of non-preserved lubricant ointment and exclude the use of lubricant drops and saline washes. We also recommend scheduled ocular surface assessments for purulent discharge, conjunctival hyperemia, chemosis and corneal opacities, any of which would indicate the need for ophthalmology consultation.

Amy Basilious

Recognizing the ocular significance: Multiple Myeloma and MGUS associated keratopathy

Kailun Jiang, Bruce D. Nichols, Paul J. Dubord, Rookaya Mather

Purpose: Corneal involvement in multiple myeloma is a rare but important manifestation of the disease. Immunoglobulin deposition in the cornea may be the first manifestation. Due to the limited number of reported cases, optimal treatment has not yet been established. Here, we report the presentation and management of 5 patients with immunotactoid keratopathy, including one case achieving complete long-term resolution of crystals.Results: We present the management of one male and four female patients with a mean age of 61 years presenting with immunotactoid keratopathy. All five presented with bilateral corneal involvement, with four having stromal crystals and one with dense peripheral stomal opacification. In three cases, visual symptoms were the

irst manifestation of their disease. All five received between 4 to 6 cycles of systemic chemotherapy with improvement in their corneal clarity, visual acuity, or both. One patient required a penetrating keratoplasty following chemotherapy, with no recurrence in the graft. One patient has maintained clear corneas 11 years after chemotherapy and autologous stem-cell transplantation and another patient maintained a visual acuity of 20/20 in both eyes 12 years after chemotherapy.Conclusions: Immunotactoid keratopathy should be considered on the differential for bilateral corneal deposits even in the absence of systemic features. Importantly, systemic therapy has the potential to improve visual outcomes, although recurrence is still possible. Future research is needed to understand disease and treatment factors that result in crystal resolution without recurrence.

Brandon Brower

Development of an In-Vitro Model of Inflammatory Bowel Disease

Mathieu Derouet, Liyue Zhang, Frederikke Larsen, Samuel Asfaha

Introduction: Inflammatory bowel disease (IBD) represents a collection of chronic intestinal diseases, primarily Crohn's disease (CD) and Ulcerative Colitis (UC). IBD is often studied in-vitro using epithelial-only intestinal organoids, but their lack of stroma limits our ability to study epithelial-mesenchymal/immune cell interactions. In contrast, Air-Liquid Interface (ALI) organoids contain all intestinal layers. ALI organoids have only thus far been described from tumor and neonatal mouse intestine. Thus, our goal is to use ALI organoids to encapsulate both epithelial and stromal components of healthy and diseased states of the adult mouse colon. Methods: Following the previously established ALI organoid protocol, we generated small intestinal and colonic ALI organoids from both neonatal (<1 week old) and adult (4-6 week old) mice. Finally, adult mice were administered 2.5% dextran sodium sulfate (DSS) for 5 days to induce colitis. 10 days following cessation of DSS treatment, we generated colonic ALI organoids which we followed using stereo and bright-field microscopy and assessed via H&E staining of formalin-fixed paraffin embedded sections. To improve culture efficiency, addition of various stem cell growth factors to the culture medium are being examined.Results: Neonatal and adult ALI organoids appear to encapsulate both epithelial and stromal components consistent with native tissue; however, we have observed a drop in efficiency in adult relative to neonatal tissue. Our preliminary data suggests addition of Wnt3a to adult cultures significantly improves efficiency of ALI organoid generation. Additionally, colonic ALI organoids generated from mice post-colitis appear to contain both epithelial and stromal components.

Evan Brydges

Tracheobronchial Involvement in granulomatosis with polyangiitis - a case series

Lillian Barra

Granulomatosis with polyangiitis (GPA) is a multisystem inflammatory disease characterized by necrotizing vasculitis predominantly in the upper and lower airways, lungs, and kidneys. Tracheobronchial stenosis is only seen in 5-12% of patients1,2,3,4 while findings such as tracheal inflammation, tracheobronchitis, inflammatory pseudo tumors and tracheomalacia4,5 have also been reported but are rare. Here, we describe the characteristics, treatments, and outcomes of 4 GPA patients with tracheobronchial involvement. All patients were female with a mean age of 38 years. 3/4 patients had tracheal involvement, 2/4 had large bronchial involvement and 3/4 had involvement of the small/medium bronchi. Antineutrophil cytoplasm antibodies were proteinase 3-positive in 2 patients, while the other 2 patients were myeloperoxidase positive. Other organ involvement was limited to the ears nose and throat, most notably hearing loss in 2/4 patients. Induction therapy involved high dose corticosteroids and either rituximab, cyclophosphamide, or azathioprine (in a pregnant patient) while rituximab was the preferred agent for maintenance therapy achieving remission in 3/3 patients. Surgical therapy involved both tracheal and bronchial dilations with 1 patient having local corticosteroid injections. Two of the patients had 1 minor relapse while 1 patient had a severe relapse leading to tracheostomy with subsequent cricotracheal resection. Our findings are similar to previous studies indicating tracheobronchial involvement typically involves younger, female patients. Our population all had responses to systemic therapy with rituximab achieving remission in 3/3 patients, while surgery was limited to simple balloon dilation treatment with good response.

Evan Brydges

Cross-Sectional Study Examining the Prevalence of Statin Use in Young Adult Patients (Age 18-39) with Diabetes Followed by the Diabetes Clinics of St. Joseph's Healthcare, London

Dr. Selena Liu, Dr. Tamara Spaic

Background: Diabetes is a major risk factor for cardiovascular disease (CVD). Although younger adults are generally not at high CVD risk, it has been shown that diabetes confers an equivalent risk as aging 15 years. In people age ≥40 years with type 1 diabetes, there is strong evidence of the benefit of statins for primary CVD prevention. However, although statins are safe and effective for cholesterol-lowering in younger individuals, the prevalence of statin use in young adults with type 1 diabetes is very low, ranging from <1%-3%. Current clinical practice guideline recommendations for statins in adults age <40 years with diabetes are weak (Grade D level evidence/consensus). It was our impression that statins may be underutilized in young adults age <40 years with

type 1 diabetes. The primary study objective was to determine the prevalence of statin use in young adults with type 1 diabetes followed in the Diabetes Clinics of St. Joseph's Healthcare London (SJHC). Secondary objectives include determining predictors of statin use in this population.Methods: This is a single centre cross-sectional study of records of patients age 18-39 years with type 1 diabetes contained in WebDR, the electronic medical record database of the SJHC Diabetes Clinics.Results: Data analysis is in progress. Descriptive statistics will be summarized and multivariable analysis performed to determine predictors of statin use.Conclusions: Results of this study will confirm whether a care gap in statin therapy in young adults with type 1 diabetes exists, and identify factors associated with statin use

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Rushil Chaudhary (Jordan Ho)

Development of a convolutional neural network to identify pleural effusion on lung ultrasound: a deep learning study

Jordan Ho, Jaswin Hargun, Chintan Dave, Derek Wu, Brian Li, Bennett VanBerlo, Jared Tschirhart, Alex Ford, Joseph McCauley, Benjamin Wu, Jason Deglint, Robert Arntfield

Point-of-care lung ultrasound (LUS) enables rapid diagnosis and management in numerous clinical settings. Identification and classification of pleural effusions in a critical care setting allows for prompt management decisions at the bedside. Lung ultrasound is especially beneficial compared to alternative imaging modalities as it allows the clinician to ascertain pleural size and guide therapeutic decisions based on imaging criteria. The goal of our project is to use deep learning methodology to rapidly identify and characterize pleural effusions during LUS image acquisition. We designed a convolutional neural network trained on LUS images from our centre demonstrating pleural effusions of different etiologies. The model will train on 200 LUS videos from patients with moderate sized pleural effusions. The trained network may further be able to classify the size and categorize the pleural effusion into simple or complex effusion. The implications of this work could allow for eventual integration of machine learning algorithms at the bedside to achieve real-time, point-of-care diagnosis, and prognosis of pleural effusion or other respiratory illnesses.

John Choi

Optimizing infliximab therapy using intestinal tissue for patients with ulcerative colitis

Dr. Reena Khanna, Dr. Aze Wilson

Background: It has been reported that up to 40% of patients with inflammatory bowel disease (IBD) will lose response to infliximab (IFX) therapy despite observing therapeutic levels of IFX in their blood samples. We aimed to determine whether tissue

concentrations of IFX could be measured precisely and whether mucosal inflammatory activity impacts the correlation between plasma and tissue concentrations of IFX.Methods: Blood samples and two adjacent sigmoid colon biopsies were obtained from 16 ulcerative colitis patients undergoing IFX therapy. Plasma and tissue biopsy concentrations of IFX were determined via a colorimetric ELISA. Disease remission and mucosal inflammatory activity were determined according to the histological findings of the pathologist. Intraindividual variability in IFX levels between adjacent biopsies were determined through paired two-tailed t-tests. A Spearman's rank correlation test was conducted to determine the correlation between serum IFX concentrations and either inflamed or uninflamed tissue concentrations of IFX.Results: No significant differences were observed between intraindividual adjacent biopsies for patients with inflamed tissue samples ($p=0.2500$) and also for patients with uninflamed tissue samples ($p>0.9999$). Additionally, a significant positive correlation between plasma and uninflamed tissue IFX levels was observed ($r=0.8068$, $p<0.0001$), however, no correlation was observed between plasma and inflamed tissue IFX levels ($r=-0.2963$, $p=0.4054$).Conclusions: Our findings suggest that plasma and tissue compartments may be interchangeable in regards to measuring IFX levels given that there is minimal mucosal inflammatory activity as assessed by histological findings. Further study with more participants are required to make firm conclusions.

Mitchell Cooper

Senior medical resident practice variability in problem list construction

Nicole Hugel, Mark Goldszmidt

Admitting a patient from the emergency department to the medical service is a critical moment in patient care and safety. Senior medical residents (SMRs) must work with junior learners overnight to assess patients and construct problem lists, all while balancing competing demands for attention. Incomplete or inaccurate problem lists constructed overnight can negatively impact patient safety or continued care by the CTU team thereafter. A deeper understanding of variability in SMR problem list construction will help provide a framework for medical educators to better teach specific methods for effective problem list creation. This study aims to investigate how SMRs construct their problem list, and explore the reviewing process between SMRs and junior learners. The study is a qualitative observational study using established constructivist grounded theory methodology. Study subjects will be SMRs and junior trainees during the overnight on-call period for CTU. Field notes, audio-recorded field interviews, and de-identified admission notes are currently being obtained for data analysis. Rhetorical genre theory and data-frame theory of sensemaking will be used for initial data analysis, with iterative phases of collection and analysis. To date, we have observed a total of 7 SMRs and 16 case reviews. We anticipate having enrolled approximately 15 SMRs by May 2022. Preliminary findings suggest SMRs uniformly

prioritize acute issues, particularly the chief presenting complaint, in their problem lists; however, there is variance between SMRs in including chronic issues. Although our findings are early, they may inform medical educators on how to approach teaching effective problem list creation.

Kaviya Devaraja

The role of ICAM1 in glioblastoma tumor associated macrophages under hypoxic conditions.

Authors: Kaviya Devaraja1, Olivia Singh2, Hafsah Ali2, Sheila Mansouri2, Gelareh Zadeh3 1. University of Toronto – Institute of Medical Science 2. MacFeeters-Hamilton Center for Neuro-Oncology Research 3. Head, Division of Neurosurgery, Toronto Western Ho

Background: Glioblastoma (GBM) is an aggressive and highly fatal brain cancer in adults. Existing treatment methods are ineffective and we are in need of new treatments that extend the overall survival and improve quality-of-life. Intracellular adhesion molecule 1 (ICAM1) is a cell adhesion molecule expressed by tumor associated macrophages (TAMs) in GBM. TAMs are thought to enhance tumor growth and proliferation, particularly within the characteristic hypoxic tumor microenvironment (TME) of GBM. Methods: Assess the expression levels of ICAM1 in primary and immortalized human and mouse macrophages under hypoxic conditions (1% O2, 0.2% O2, and HIF stabilizing drug IOX4). Analyze the effect of ICAM1 deficiency, down-regulation, and over-expression on macrophage behaviour including migration, proliferation, phagocytosis and adhesion to co-cultured tumor cells. Intracranially inject ICAM1 knockout mouse model with GBM tumor cells and analyze tumor growth, overall survival of the mice, and the composition of the tumor microenvironment. Results: ICAM1 is highly expressed in different cell types within GBM. The expression is enhanced when macrophages are treated with tumor cell-conditioned medium in vitro and is further exacerbated upon incubation of these cells in a hypoxia. The migration levels of macrophages is higher in wild type cells than in ICAM1 deficient cells and increases upon treatment with tumor cell-conditioned medium and hypoxic conditions. ICAM1 deficient mice succumbed more quickly to GBM than wild type mice. Conclusions: The expression of ICAM1 in TAMs in hypoxic TME promotes GBM cell invasiveness and migration. ICAM1 can be targeted as a treatment method to improve patient survival.

Chris Earle

Efficacy of a manualized virtual Cognitive Behavioral Therapy for Insomnia group intervention

Dr. Chris Earle

Background: Cognitive behavioral therapy for insomnia (CBT-I) is the preferred treatment for chronic insomnia but demand exceeds availability. Virtual and group treatments may increase access, but their efficacy has not been well-established. Objective: We assessed the efficacy of a virtual group CBT-I facilitated book-club program at LHSC. Methods: 23 participants (mean age = 55.0 y, SD 12.7, 91% female) with insomnia disorder were recruited. Data from 14 individual CBT-I patients was used to establish comparative efficacy. Groups showed no differences in baseline measures. The group intervention consisted of 7 weekly sessions with 6 hours of patient contact in groups of 7-10 participants. Individual therapy ran for 6-8 sessions with 4.5 hours of contact per patient. Measures: Primary outcome was Insomnia Severity Index (ISI) at pre-/post-treatment. Secondary measures included depression (PHQ9), anxiety (GAD7), and disability (SDS). Sleep diaries measured Sleep Latency (SL), Wake After Sleep Onset (WASO), Total Sleep Time (TST), and Sleep Efficiency (SE). Results: CBT-I group intervention showed significant improvement in insomnia severity (mean difference 11.8, $p < 0.001$, Cohens d 2.220). There were significant improvements in PHQ9, GAD7, SDS, SL, WASO, TST, and SE with large effect sizes. Group treatment showed comparable effect sizes to individual therapy for all measures with significantly greater improvements seen in depression and anxiety symptom severity. Conclusions: These findings support use of virtual group CBT-I. Group therapy showed similar effect size to individual therapy. Benefits of virtual group therapy included reduced cost, resource utilization, and better efficiency of delivery. Further randomized studies are required to determine transferability to other settings

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Reidun Garapick

Paramedics' ability to determine diagnosis and most appropriate destination in patients who activate 9-1-1.

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Alternative destination pathways provide an opportunity for redirection of low-acuity 9-1-1 patients away from emergency departments (EDs). This study analyzes the accuracy of suspected diagnoses made by paramedics and their ability to identify appropriate destinations for patients. At patient handover, paramedics recorded their suspected diagnosis and if an alternative destination would have been suitable. Two ED/EMS

physicians determined the accuracy of the paramedic's suspected diagnosis by comparing it with the ED diagnosis and determined if the alternative destination was suitable. A third ED/EMS physician was used when agreement did not exist. 493 patient transfers were included. 329 (66.73%) suspected diagnoses were deemed a 'reasonable match', 126 (25.56%) were a 'miss', and 38 (7.71%) were a 'critical miss' (high-morbidity pathology present but not identified). Of cases (n=161) in which paramedics suggested an alternative destination, 58 (51.33%) 'matches', 24 (64.86%) 'misses', and 11 (100%) 'critical misses' were redirected to an inappropriate destination. Of the inappropriate destinations (n=93), the most common were to a family physician (35.5%), urgent care centre (33.3%), and release from care with no follow-up (15.1%). This demonstrates a high proportion of incorrect suspected diagnoses and inappropriate destination decisions by paramedics. This introduces a risk for redirection of high-acuity patients away from the ED to alternate centres unable to provide the required care. While alternative destination pathways remain one potential solution to overcrowded EDs, further training and use of robust directives may be required for paramedics to accurately identify low-risk patients that could be safely redirected from the ED.

Artin Ghassemian

Reducing pleural fluid flow cytometry testing - shared decision making between the clinic and laboratory

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Background: Pleural fluid flow cytometry is commonly ordered in the investigation of pleural effusions, with evidence suggesting it may be overutilized. The goals of this study were to determine the pleural fluid flow cytometry positivity rate at our institution and develop a screening algorithm to reduce low-yield testing. Methods: We reviewed 100 pleural fluid flow cytometry orders between January-July 2020 and the electronic patient record for clinical history and pleural biochemistries. We developed and back-tested an algorithm with two components: 1) clinical criteria: flow indicated for active or suspected hematologic malignancy and not indicated in patients with active solid tumor malignancy or palliative thoracentesis, and 2) presence of any of the following would rule out the need for flow cytometry: fluid cell count <0.3x10^9/L, fluid glucose <0.2 mmol/L, transudative effusion by Light's criteria, or recent negative pleural fluid flow cytometry. Results: We identified fourteen flow-positive tests, of which four were new diagnoses. Back-testing our screening algorithm showed a sensitivity of 100% in identifying flow-positive pleural samples and would have led to a 41% reduction in flow cytometry testing without missing any positive results. Discussion: Our algorithm is a novel example of Shared Decision Making between laboratory and clinician, acknowledging both clinical uncertainty at the bedside and expertise in the laboratory

allowing for canceling specialized testing if deemed unnecessary by objective criteria. We plan to prospectively evaluate the screening algorithm within our institution and study outcomes of our intervention on number of monthly pleural fluid flow cytometry orders and cost avoidance.

Christopher Goy

Adverse events in alternate-level of care (ALC) patients awaiting long-term care (LTC) as compared to patients in LTC.

Lim Fat, GuillaumeLee, PaulDawson, EmilyTaabazuing, Mary Margaret

Patients who have not secured a place in Long Term Care (LTC) often wait in hospital and are designated as an alternate-level of care (ALC). There exists limited data about the adverse events these patients experience and how they compared to adverse events that occur to those who are in LTC. Accordingly, we have sought out to compare the rate and character of adverse events in LTC patients as compared to ALC patients awaiting LTC in hospital. Using a retrospective observational method, we systematically investigated 150 randomly sampled patient records for each patient's first 150 days at a local LTC facility. We recorded baseline conditions as well as infectious and non-infectious adverse events. Infectious adverse events comprised of respiratory infections, urinary infections, gastrointestinal infections, and skin/soft tissue infections. Non-infectious adverse events comprised of falls, delirium, pressure ulcers and venous-thrombotic events. Our preliminary LTC data demonstrated 137 total infectious events and 383 total non-infectious events in LTC as compared to 94 infectious adverse events and 268 non-infectious events in hospitalized ALC patients. The increased non-infectious events in the LTC group was related to a higher number of falls documented. The direct comparison of these two groups and the difference in their adverse events helps clarify the implications of waiting in hospital for LTC. This data informs considerations about health care cost, resource management, and patient outcomes.

Emma Graham

E-cigarette vapour impairs pulmonary surfactant

Lynda McCaig, Gloria Sui-Kei Lau, Akash Tejura, Anne Cao, Ruud Veldhuizen

The use of electronic cigarettes (ECs) continues to increase especially amongst young populations, in part due to the wide variety of devices and flavour available. However, it can also lead to lung injury. During deep inhalation, the first compound EC vapour interacts within the alveoli is pulmonary surfactant. This mixture of lipids and proteins lines the alveolar surface and reduces surface tension thereby providing alveolar stability and ease of breathing. Impairment of surfactant's surface tension reducing activity will contribute to lung dysfunction. Numerous case studies report incidences of

vaping associated lung injury (EVALI), and even death, however vaping remains popular. Hypothesis: Exposure to EC vapour will disrupt surfactant's ability to reduce alveolar surface tension leading to lung injury. Methods: Bovine lipid extract surfactant (BLES) (2ml at 2mg/ml) was exposed to various EC vapours differing in flavour and nicotine content. The ability of the exposed surfactants to reduce surface tension was analysed on a constrained sessile drop surfactometer. Results: Minimum surface tensions increased after exposure to vapour as compared to non-exposed surfactant. Variations in device used, addition of nicotine, or temperature of vapour had no additional effect. Out of 10 flavours tested, only menthol and red wedding flavoured e-liquid had further detrimental effects. Conclusions: It is concluded that one of the harmful effects of e-cigarette use is impairment of the pulmonary surfactant system. We speculate that this surfactant impairment makes the lung more susceptible to injury.

Matthew Greenacre

Validation of Pneumocystis Pneumonia Diagnostic Codes in Ontario

Yael CampanileSasan HosseiniMichael Silverman

The large ICES database is a very promising tool for answering epidemiological and clinical questions about infectious diseases. For example, Pneumocystis pneumonia (PCP) is a fungal infection that afflicts patients with significant immunocompromise. Initially described in HIV/AIDS, it is also a cause of morbidity and mortality in patients with hematologic malignancies and on post-transplant immunosuppression. In this study, we reviewed the charts of patients tested for PCP to determine whether PCP testing is positive or negative, and whether their is clinical evidence of plausible PCP infection. Documented microbiological evidence of PCP is set as the gold standard against which we estimate the signal detection parameters for ICD-10 Codes for PCP. Results of this study are currently pending.

Fahad Hannan

Investigating the Effect of Thrombotic Thrombocytopenic Purpura on Neurocognitive Function

Dr. Jonathan D. Thiessen, Dr. Susan HS. Huang, Dr. Michael Jurkiewicz

There have been numerous studies done that report increased risk of stroke, depression, and cognitive impairment in patients with Thrombotic Thrombocytopenic Purpura (TTP) post remission. TTP is a hematological disease arising from antibody-mediated inhibition of a crucial protein that monitors blood clotting in the microvasculature. The reduced activity of this protein allows for unregulated spontaneous clotting which can lead to death if not treated immediately. However, while studies indicate health risks for patients in remission, structural changes in the brain

caused by TTP has not been thoroughly investigated. A potential cause for these increased risks may arise from an increase in the blood brain barrier (BBB) permeability which signifies a leakage of blood in the brain. Pathogens and toxins from the blood may contribute to neuroinflammation, an early hallmark symptom of cognitive decline. By using quantitative and qualitative magnetic resonance imaging (MRI), patients were found to have numerous white matter hyperintensities along with increased T1 and T2 relaxation times in the frontal lobe and cingulate cortex. These correlate with findings from a depression score using the Montgomery-Åsberg Depression Rating Scale (MADRS) which report concentration difficulties, lassitude, and anxiety. As well as a cognitive assessment from Cambridge Brain Sciences (CBS) which show decreased scores in short-term memory, attention, concentration, and mental manipulation. White matter changes detected with MRI may be attributed to neuroinflammation, ischemia, or infarction in these regions but further investigation with additional MRI techniques is needed to substantiate these results.

Malek B. Hannouf

Real-world impact of TAILORx on chemotherapy use and SOFT/TEXT on ovarian function suppression uptake in women 40 years and under with HR-positive, HER2-negative, axillary lymph node negative breast cancer in Alberta, Canada

Muriel Brackstone, Kim Koczka, Sasha Lupichuk

Gene expression profiling (GEP) testing is prognostic for distant recurrence risk in women with hormone receptor positive (HR+), human epidermal growth factor receptor-2 negative (HER2-), axillary lymph node negative (LN-) breast cancer. The TAILORx trial generated prospective evidence demonstrating GEP is also predictive of chemotherapy (CT) benefit, promising to reduce adjuvant CT prescription. In the same era, the SOFT/TEXT trials demonstrated disease-free survival benefit for the addition of ovarian function suppression (OFS) to tamoxifen or exemestane versus tamoxifen alone in women remaining premenopausal following CT. Real-world uptake and impact of these advances in the management of HR+, HER2-, LN- breast cancer in young women is limited. This retrospective study evaluated the use of GEP, CT and OFS in all women who were 40 years of age or younger diagnosed with HR+, HER2-, LN- breast cancer during the period from 2011 to 2020 in Alberta.Patients and clinical variables were retrieved from the Alberta Health Services Cancer Care Breast Data Mart and through review of the electronic medical record. Of the 314 eligible patients, 113 (46.3%) underwent GEP testing, 182 received CT, and 55 had OFS. The frequency of GEP, CT, and OFS use will be examined yearly to evaluate the impact of various time points: funding of GEP in 2014, publication of TAILORx in 2015, funding of OFS in 2015, and publication of SOFT/TEXT in 2018. Multivariate logistic-regression analyses will evaluate the independent impact of these various time points in the uptake of these therapies, after adjusting for clincopathologic characteristics.

Cassandra Hawco

Characteristics of Women with Diabetes in Pregnancy During the COVID-19 Pandemic

Selina Liu MD FRCPCTamara Spaic MD FRCPC

St. Joseph's Hospital is the regional centre of care for diabetes in pregnancy and has been experiencing an increased referral volume in our Endocrine Pregnancy Clinic (EPC). Objective: To characterize women with diabetes in pregnancy assessed in the St. Joseph's Hospital (SJHC) EPC in the year pre-COVID (April 1, 2019-March 31, 2020) versus the first year of COVID (April 1, 2020-March 31, 2021). Method: A single-centre, retrospective cohort study of women referred to SJHC EPC for diabetes in pregnancy (type 1, type 2 or gestational) during the time period of interest. Results: 187 patient charts were reviewed, 107 (57%) pre-COVID and 80 (43%) during COVID. Most patients had gestational diabetes (86% pre-COVID, 66% during COVID), and fewer had type 2 diabetes (7% pre-COVID, 15% during COVID) or type 1 diabetes (5% pre-COVID, 16% during COVID). Most patients resided less than 50 km from London (96% pre-COVID, 85% during COVID). Mean gestational age at initial physician consultation was 27 weeks. The mean number of reassessments during pregnancy was 2 (range 0-10) for physician appointments and 10 (range 0-49) for certified diabetes educator (CDE) appointments.Conclusions: In the year pre-COVID and the first year of COVID, most women cared for in the SJHC EPC had gestational diabetes. Women had frequent contact with the EPC, mostly provided by CDEs, although there was a high range in the number of contacts. Data collection is ongoing-it is anticipated that the study results will provide important information to help future clinic care and resource planning.

Cassandra Hawco

Fibrous dysplasia treatment: a role for osteoclastogenesis inhibition

Stan Van Uum MD PhD FRCPCKristin Clemens MD MSc FRCPCMohammad Jay MD

Fibrous dysplasia (FD) is a chronic and progressive disorder of bone growth. Common symptoms include pain, fracture and uneven bone growth. Osteoclast overactivity is a part of the proposed mechanism for FD. The mainstay of treatment consists of bisphosphonates with the primary goal of pain relief. In patients refractory to bisphosphonates, Denosumab has also been shown to be effective in achieving pain control. Corticosteroids are used short-term when FD affects the vision. In March 2011, our patient presented to ophthalmology with intermittent proptosis and vertical diplopia. CT head revealed a skull base lesion which was confirmed to be fibrous dysplasia on bone biopsy. Due to her continued proptosis and significant headache, she was started on IV Pamidronate monthly for pain control in November 2011. Repeated attempts to decrease the frequency of the infusion were unsuccessful due to breakthrough pain. Oral Alendronate and Risedronate resulted in inadequate pain control. In August 2021,

she was diagnosed with metastatic melanoma and started Nivolumab while maintaining oral Risedronate for FD treatment. Since starting Nivolumab, her pain completely resolved for the first time in ten years, despite no changes to her bisphosphonate therapy. While Nivolumab, a human programmed death receptor-1 blocking antibody, has been utilized in the treatment of malignancy in bone, it has not been previously studied in FD. Nivolumab inhibits osteoclastogenesis and this mechanism has been proposed to decrease bone cancer pain. This case report suggests further research into the potential role for Nivolumab in the treatment of patients with FD is waranted.

Alexandra Hillyer

COVID-19 Vaccine Humoral Response and Treatment Effect in Patients with Hematologic Malignancy

Jordan Spradbrow, Michael J Knauer, Jenny Kim, Anthony Quint, Nicolette Joh-Carnella, Selay Lam, Husam Abdoh, Danny Dawd, Joy Mangel, Kang Howson-Jan, Anargyros Xenocostas, Uday Deotare, Lalit Saini, Alejandro Lazo-Langner, Cheryl Foster, Martha Louzada, Jenny Ho, Ian Chin-Yee,

Background: Patients with hematologic malignancies have a lower vaccine response and higher rates of SARS CoV-2 morbidity and mortality. We present preliminary data on humoral vaccine response correlation between disease subtype and treatment exposure.Methods: We performed a prospective serologic study on patients with a hematologic malignancy who received SARS-CoV-2 vaccination. We analyzed 332 patients' blood samples from May 1, 2021 - Jan 31, 2022, with the Elecsys® Anti-SARS-CoV-2-S test.Results: Median age was 67 years with 41.9% female. Treatment status at first vaccine significantly affected peak antibody response after second vaccination (2V) ($p<0.05$). Seropositive rate and median antibody titer after 2V for previously untreated patients were higher compared to patients on active therapy or had previous therapy. Treatment naïve (n=60;seropositivity 85.1%;median titer 1306U/mL); first-line (1L) therapy (n=127;65.4%;41.25U/mL); second-line and beyond (2L+) therapy (n=56; 60.7%;2.6U/mL); previous treatment with 1L (n=66;64.8%;118U/mL); previous treatment with 2L+ (n=23;59.1%;4U/mL). Of 61 patients that were seronegative at 2V, 17(27.9%) seroconverted after 3V. The most recent treatment type received from 2V impacted humoral responses. Exposure to anti-CD20 monoclonal antibody-based regimens or as monotherapy revealed the lowest antibody responses (n=84;seropositivity22.6%;median titer< 0.8U/mL). In addition, when treatment is received closer to 2V, lower responses were observed: <3months (n=33; 22%;<0.8U/mL) vs. 12-24months (n=4;60%;228U/mL).Conclusions: The humoral response from our single-institution cohort identifies diminished responses depending on treatment status and the proximity of treatment exposure to receipt of vaccination.

Zaid Hindi

Incidence and Predictors of Non-Hepatic Cancers in Alcohol Related Liver Disease in the WALDO Cohort

Mayur Brahmania, Juan Pablo Arab, Nancy Shi, Neil Rajoriya, Guruprasad P. Aithal, Michael Allison, Hannes HagstrÃ¶m, Alisa Likhitsup, Anne McCune, Steven Masson, Richard Parker

Background: Alcohol-related liver disease (ArLD) accounts for 48% of cirrhosis-related deaths in the world. Alcohol is a contributor to hepatocellular carcinoma (HCC) and non-hepatic cancers (NHC). We aimed to describe the incidence and predictors of NHC in patients with ArLD.Methods: Data came from an international, multicenter retrospective cohort study of patients with histologically characterized ArLD. We excluded all patients with evidence of liver disease due to another etiology. The primary outcome was incidence of the first NHC. To identify risk factors of NHC, baseline characteristics of patients with and without NHC were compared. Outcomes were presented as unadjusted and adjusted hazard ratios (HR) based on COX analysis.Results: 633 patients with histologically characterized ArLD were included. The mean age was 51 years, 64% of patients were male and 58% had cirrhosis on biopsy. We found that 69 patients with ArLD (11%) developed NHC during a median follow-up of 8.8 years. The most common NHC was lung cancer (19%). Patients who developed NHC were older (55 vs. 50 years old; p<0.0001). BMI, current or past smoking status, peak alcohol use, absence of cirrhosis and histological findings did not differ between groups. On multivariable analysis, past smoking status (HR 5.70, p=0.002) and current smoking status (HR 4.95; p = 0.003) were associated with higher rates of NHC. Conclusion: In this large multicenter cohort study, we found ArLD is associated with an increased incidence of NHCs, primarily lung cancer. Past and current smoking are risk factors of NHC in ArLD.

Mina Ishak

Risk of Iatrogenic Pneumothorax based on Location of Transbronchial Biopsy: A Retrospective Cohort Study

Debarati Chakraborty, Shayan Kassirian, Inderdeep Dhaliwal, Michael A. Mitchell.

Transbronchial lung biopsy is a commonly performed procedure to obtain lung tissue during flexible bronchoscopy. Pneumothorax is among the most common complications of TBB. A prior publication has reported that performing a TBB from the left upper lobe is associated with a significantly higher risk of pneumothorax. Although it is hypothesized that the apical-basal intrapleural gradient may explain this finding, these results have not been subsequently replicated. The objective of this study was to assess whether location of TBB correlated with development of post-procedural pneumothorax. We also sought to identify additional risk factors associated with

pneumothorax development. This was a single-centre, retrospective cohort study done at Western University. All TBB performed in a 10 year period (total of 222 TBB) were identified with subsequent chart review. Radiographic evidence of pneumothorax was reported in 38 patients with 10 patients requiring a chest tube. In the multivariable analysis, risk of pneumothorax was significantly higher for biopsies obtained from the left upper lobe (OR 3.33; 95% CI 1.25 - 9.06). Being an inpatient at time of procedure was also associated with a significantly increased risk of pneumothorax. Our results are consistent with a prior study demonstrating an increased risk of pneumothorax following TBB when obtained from the left upper lobe. Contrary to prior results, we found no association with BMI or number of biopsies taken. Clinicians should be aware of the increased risk of pneumothorax when performing TBB from the left upper lobe and should consider alternative locations in patients with diffuse lung disease.

Tyler James

Ring Sideroblast Quantification in Patients with SF3B1 Mutation and Myelodysplastic Syndrome: A Retrospective Chart Review

Benjamin Chin-Yee, Bekim Sadikovic, Ben Hedley, Ian Chin-Yee, Cyrus Hsia

Introduction: Myelodysplastic syndrome (MDS) occurs when impaired hematopoiesis causes dysplastic cytopenias potentially causing blood transfusion dependency. MDS with ring sideroblasts (MDS-RS) is a subtype diagnosed on bone marrow aspirate when either i) ≥15% of erythroid precursors are ring sideroblasts or ii) 5-14% ring sideroblasts and the SF3B1 mutation. In 2020, the MEDALIST trial showed MDS-RS subtype patients have decreased transfusion dependency with Luspatercept. However, ring sideroblasts are routinely only reported when ≥15% and the SF3B1 mutation is not routinely tested. Therefore, patients with SF3B1 mutations and 5-14% ring sideroblasts are commonly not identified for eligibility for Luspatercept. Unlike other Canadian centers, London Health Sciences completes genetic testing on all bone marrow specimens for MDS which includes the SF3B1 mutation. We are uniquely poised to identify all MDS-RS patients given this advanced testing. Methods: The Next Generation Sequencing (NGS) database was used to select MDS patients from 2018-2020 that possess the SF3B1 mutation. The bone marrow aspirates will be reviewed by a pathologist to enumerate ring sideroblasts.Results: Of the 2023 patients in the NGS database, 167 patients have MDS. Twenty-three have the SF3B1 mutation, which includes 16 patients already identified as having ≥15% ringed sideroblasts. We will next enumerate ring sideroblasts for the remaining 7 patients.Conclusion: This work aims to quantify patients currently being missed by Canadian laboratory reporting practices that may benefit from Luspatercept to reduce blood transfusion dependency. This group may represent as high as 30% of MDS patients with SF3B1 mutations.

Gabriel Jeyasingham

Relapses and Serious Complications in ANCA-Associated Vasculitis Patients with End-Stage Renal Disease

Dr. Susan HuangDr. Lakshman GunaratnamDr. Lillian Barra

Anti-neutrophilic cytoplasmic antibody-associated vasculitis (AAV) is a rare multisystem autoimmune disease. Renal involvement is common and an important predictor of mortality. Early treatment and maintenance with immunosuppression are required to prevent complications and relapses of severe AAV. However, for AAV patients with end-stage renal disease (ESRD), severe infections are the major cause of death. When prescribing immunosuppression, the need to prevent other AAV-related disease complications must be weighed against the risk of increasing infections. Outcomes for patients with AAV-related ESRD in Canada have not previously been reported and optimal management of these patients is unclear. The objective of this study is to describe outcomes and complications in AAV patients on chronic dialysis or undergoing renal transplantation in Canada. A Canadian multi-centre case series will retrospectively include patients ≥ 18 years old with AAV and ESRD requiring renal replacement therapy ≥ 6 months or renal transplantation. Outcomes will include rates of major relapse, serious infection, cardiovascular events, malignancy and all-cause mortality. Descriptive statistics will be used to report patient characteristics and outcomes. At the Western University site, 8 patients have been identified with median age 57 and 62.5% being female. Six receive chronic dialysis and two underwent renal transplant. We expect another 50 patients from the other 5 sites. Preliminary results suggest that relapses before initiation of dialysis and infections are common in patients with AAV who go on to develop ESRD. We expect relapses to decrease, but infectious and cardiovascular complications to increase after ESRD.

Tharsan Kanagalingam

Protocol to reduce the risk of denosumab induced hypocalcemia

Cindy Hoy, Tayyab Khan, Nabil Sultan, Andrea Cowan,Jenny Thain, Kristin Clemens.

Background: Fracture prevention in patients with advanced CKD poses a unique challenge. Traditional anti-resorptive medications (i.e., bisphosphonates), are contraindicated in CKD. While denosumab is used in advanced CKD, it can cause drug-induced hypocalcemia. Thus, patient management needs to be standardized to improve outcomes. Method: We are carrying out a multidisciplinary (nursing, endocrinology, nephrology), quality improvement initiative for patients with advanced CKD (GFR <30ml/min/1.73m2) prescribed denosumab for Osteoporosis at St. Joseph's Hospital. Using a structured algorithm focused upon optimizing CKD-MBD prior to denosumab therapy, and calcium and vitamin D prophylaxis and post injection serum corrected calcium level monitoring, we aim to reduce the risk of denosumab-induced

hypocalcemia by 30% over 1 year. Our primary outcome measure will be percentage of patients with denosumab-induced hypocalcemia (corrected calcium <1.9mmol/L) within 8 weeks of treatment. Process measures include adherence with calcium, vitamin D and monitoring. Balance measures include the percentage of patients with hyperphosphatemia (phosphate >1.8mmol/L) and hypercalcemia (corrected calcium >3.0 mmol/L). We will use QI methods (Pareto, Run Charts) to analyze data.Results: Baseline data demonstrated 4/8 patients (50%) (5 with GFR <30ml/min/1.73m3, 3 on dialysis) treated with denosumab prior to our intervention experienced hypocalcemia. Post initiation of our protocol, no cases of hypocalcemia were observed in 15 patients (12 with GFR <30ml/min/1.73m3 and, 3 on dialysis)Discussion: To date, we have not observed hypocalcemia after initiation of the standardized protocol in patients' part of St. Joseph's Osteoporosis and Metabolic Bone Disease Program. Data collection will continue until Feb 2023.

Shayan Kassirian

Diagnostic Sensitivity of Pleural Fluid Cytology in Malignant Pleural Effusions: Systematic Review and Meta-analysis.

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Background: Pleural fluid cytology is an important diagnostic test used for the investigation of pleural effusions. There is considerable variability in the reported sensitivity for the diagnosis of malignant pleural effusions (MPE) in the literature. Objective: The purpose of this review is to determine the diagnostic sensitivity of pleural fluid cytology for MPE to better inform the decision-making process when investigating pleural effusions. Data sources: A literature search of EMBASE and MEDLINE was performed by four reviewers. Articles satisfying inclusion criteria were evaluated for bias using the QUADAS-2 tool. Data extraction: For quantitative analysis, we performed a meta-analysis using a binary random-effects model to determine pooled sensitivity. Subgroup analysis was performed based on primary cancer site and meta-regression by year of publication.Synthesis: Thirty-six studies with 6057 patients with MPE were included in the meta-analysis. The overall diagnostic sensitivity of pleural fluid cytology for MPE was 58.2% (95% CI 52.5% - 63.9%; range 20.5% - 86.0%). There was substantial heterogeneity present amongst studies (I2 95.5%). For primary thoracic malignancies, sensitivity was highest in lung adenocarcinoma (83.6%; 95% CI 77.7% - 89.6%) and lowest in lung squamous cell carcinoma (24.2%; 95% CI 17.0% - 31.5%) and mesothelioma (28.9%; 95% CI 16.2% - 41.5%). For malignancies with extra-thoracic origin, sensitivity was high for ovarian cancer (85.2%; 95% CI 74.2% - 96.1%) and modest for breast cancer (65.3%; 95% CI 49.8% - 80.8%). Conclusions: Clinicians

should be aware of the high variability in diagnostic sensitivity by primary tumour type as well as the potential reasons for false-negative cytology results.

Nadine Khalil

Erythema multiforme major precipitated by orolabial and conjunctival Herpes Simplex Virus-1 reactivation

Dr. Megan Devlin

BackgroundHerpes associated erythema multiforme (HAEM) is an exudative cutaneous and/or mucosal hypersensitivity reaction caused by Herpes Simplex Virus 1 or 2. We present a case of HAEM with extensive skin and mucosal involvement.CaseA 72-year-old woman presented to hospital with redness surrounding her eyes and eye itchiness. Her past medical history included hysterectomy and previous HSV-1 oral lesions. She was thought to have pre-septal cellulitis and was started on Amoxicillin-Clavulanic Acid. Subsequently, she developed a targetoid papular rash on her hands, mouth, and upper and lower extremities. Steven Johnson Syndrome was on the differential diagnosis and she was given 3 doses of IVIG. IV acyclovir was later administered as her rash was later thought to be erythema multiforme from HSV reactivation. On physical exam, she was febrile at 38.7 degrees Celsius, but hemodynamically stable. She had well-circumscribed, violaceous, targetoid lesions with scaly plaques affecting the periorbital region, cheeks, mouth and extremities. She had significant involvement of the hands, particularly the fingertips. Viral swabs of her oral and eye regions were positive for HSV-1 and other infectious work up negative. Skin biopsy of a lesion was non-conclusive, noting mild spongiosis and no viral cytopathic effect. The patient was treated with 21 days of initially IV acyclovir, then valacyclovir with improvement.ConclusionThe patient was diagnosed with erythema multiforme triggered by orolabial and conjunctival HSV reactivation and improved with systemic antiviral therapy. In severe cases such as these, other diagnoses such as SJS should be considered in the differential diagnosis.

Adrian Kuchtaruk

Unplanned Readmissions after Impella Mechanical Circulatory Support

Rodrigo Bagur, MD, PhD

BACKGROUND: Early readmissions significantly impact patient-wellbeing and health-care financial burden. Data on 30-day readmissions following Impella mechanical circulatory support (MCS) implantation are unknown.OBJECTIVES: To assess the rates, causes and factors associated with 30-day unplanned readmissions after Impella MCS.METHODS: Discharged patients who underwent Impella MCS between January 2016 and November 2019 in the U.S. Nationwide Readmission Database were analyzed. Incidence, causes, and factors associated with 30-day readmissions were

assessed.RESULTS: Of 22,055 patients who required Impella MCS, 2,685 (12.2%) were readmitted within 30 days with 70% readmitted to the index hospital. Readmitted patients were significantly older (median age 71 vs. 68 years), more likely to be female (31% vs. 26%) and had a shorter length-of-stay (index hospitalization, median 8 vs. 9 days). The factors associated with 30-day readmissions were discharge against medical advice (adjusted odds ratio [aOR]: 2.06, 95% confidence interval [95%CI]: 1.37-3.09, P=0.001), same state resident (aOR: 2.04, 95%CI: 1.76-2.36, P<0.001), renal disease (aOR: 1.46, 95%CI: 1.35-1.57, P<0.001), liver disease (aOR: 1.38, 95%CI: 1.17-1.63, P<0.001), chronic pulmonary disease (aOR: 1.23, 95%CI: 1.15-1.33, P<0.001), female gender (aOR: 1.21, 95%CI: 1.12-1.30, P<0.001), and STEMI diagnosis on admission (aOR: 1.16, 95%CI: 1.02-1.31, P=0.03), among others. There was an even split between cardiac (49.9%) and non-cardiac readmissions (50.1%).CONCLUSIONS: Thirty-day readmissions after Impella MCS are relatively common and relate to sex, baseline comorbidities, insurance coverage, and length of hospital stay.

Frederikke Larsen

DNA Hypomethylation Inhibits Tuft Cell-Derived Colitis-Associated Cancer

Hayley Good, Alice Shin1, Liyue Zhang, Samuel Asfaha

Introduction: Colorectal cancer is the second leading cause of cancer death in Canada. A major risk factor for the development of colorectal cancer is chronic inflammation. We previously described a colitis-associated cancer (CAC) mouse model in which tumors arise from DCLK1+ tuft cells following loss of the tumor suppressor adenomatous polyposis coli (APC) and colitis induction. Interestingly, epithelial cells in colitis and CAC display DNA methylation changes, but the effect of these changes on colonic tumorigenesis is unknown. Thus, we hypothesized that inhibition of DNA methylation in DCLK1+ tuft cells reduces colonic tumorigenesis. Methods: We induced CAC in Dclk1/Apcf/f and Dclk1/Apcf/f/Dnmt1f/f mice by administering tamoxifen to induce APC and DNMT1 gene loss followed by 2.5% dextran sodium sulfate to induce colitis. Fourteen weeks later, we assessed colonic tumor number and size. In a separate cohort of Dclk1/Apcf/f mice, we induced CAC and treated the mice with the DNA de-methylating drug 5-AZA-2'-deoxycytidine (5-AZA). Lineage tracing from DCLK1+ cells was examined from all mice.Results: DNMT1 deletion in DCLK1+ cells or treatment with 5-AZA significantly inhibited the number and size of colonic tumors. Interestingly, single DCLK1+ cells that did not lineage trace were detected in 5-AZA treated mice. Deletion of DNMT1 or 5-AZA treatment additionally reduced the number of lineage tracing events detected upon exposure to low dose DSS. Discussion: Our findings demonstrate that DNMT1 loss or 5-AZA treatment inhibits CAC and tuft cells stemness, suggesting that DNA hypomethylation plays an important role in colitis-associated tumorigenesis.

Derek Little

Effectiveness of Balloon-occluded Retrograde Transvenous Obliteration for Primary Prophylaxis of Gastric Variceal Bleeding: A Systematic Review

Nisha Howarth MD FRCPC, Mayur Brahmania MD MPH

Introduction: Balloon-occluded retrograde transvenous obliteration (BRTO) is an effective treatment to prevent rebleeding from gastric varices (GV). Its role in primary prophylaxis has not been established. Objectives: To determine the effectiveness of BRTO for primary prophylaxis of GV bleeding. Methods: We searched EMBASE, MEDLINE and the Cochrane Central Register of Controlled Trials from inception to November 2021. Randomized controlled trials and observational studies involving adults with cirrhosis related GV that have never bled and treated with BRTO were included. Studies without clinical outcomes or those not reporting primary prophylaxis outcomes separately were excluded. Risk of bias was assessed using the Newcastle-Ottawa scale. Results: We identified 790 unique citations with 9 eligible studies after full-text review. A total of 577 patients were included from 9 observational studies (1 prospective, 8 retrospective). Technical success after the first procedure ranged from 82.4-100% (7 studies) and GV eradication on follow-up endoscopy ranged from 88.2-100% (4 studies). GV bleeding occurred in 0-10.0% of patients with follow-up ranging from 15.8-66.2 months (9 studies). Eight studies were considered at high risk of bias due to the lack of a control group or poor comparability between the cohorts. Conclusions: BRTO appears to be effective for primary prophylaxis of GV bleeding. Further controlled studies are needed before BRTO can be routinely performed for primary prevention of gastric variceal bleeding.

Jessica Liu

Eosinophilic inflammatory phenotype and treatment response to biologics in patients with ulcerative colitis: A retrospective cohort study

Jason Chambers BSc, Lisa Cameron PhD, and Aze Wilson MD PhD

Background: Peripheral eosinophilia in ulcerative colitis (UC) has been associated with increased severity of disease presentation and increased risk of surgery. However, the link between inflammatory phenotype and treatment response is not well defined. We aimed to evaluate inflammatory phenotype using eosinophils as a surrogate marker of Th2 inflammation and response to biologic treatment in patients with UC.Methods: A retrospective cohort study was conducted on patients with UC from the London Health Sciences Centre. Participant data was collected from charts at diagnosis, and before and after the initiation of corticosteroid and biologic treatment. Disease activity was assessed using the Mayo index and histology on endoscopic biopsy was captured at the time of blood collection. Participants were categorized into high (≥ 150/μL) or low (< 150/μL) eosinophil groups based on their eosinophil count prior to exposure to any

systemically immunosuppressive agents. Fisher's exact tests were used to compare categorical variables between the groups.Results: High eosinophil counts were associated with increased rates of dose escalation of infliximab to attain disease remission, compared to low eosinophil counts (OR = 9.60, 95% CI = 1.078 to 115.8, p = 0.039). There were no differences in rates of remission on infliximab or on anti-TNF agents overall, hospitalizations, or surgical resection between the two groups.Conclusion: Our data suggests that patients with high eosinophil phenotype are more likely to require dose escalation of infliximab to attain remission in UC. Further investigation is required to understand the effect of inflammatory phenotype on individual response to biologic treatment.

HAITAO LU

CaMKs interactively regulate Drp1 in mediating necroptosis and inducing heart transplantation rejection

Patrick McLeod, Xuyan Huang, Zhu-Xu Zhang

Mitochondrial dysfunction is associated with organ transplantation rejection and poor allograft prognosis. Activated Drp1 is one of important contributions to damaged mitochondria. During fission, elevated Ca2+ intake and decreased ATP showed the relationship with CaMKs family proteins. CaMK2 was activated by RIPK3 to mediate cell death signals; in addition, CaMK1/CaMK4 had functions on activation of CaMK2. Therefore, we hypothesized that interactions among CaMK1/2/4 regulate Drp1 as necroptosis and induce heart transplantation rejection.Methods. In vitro, we used cell death assay to confirm the role of Drp1 and CaMKs in necroptosis. Next, we determined the activation of Drp1 by CaMK1 or CaMK2 by Western Blotting in camk1 and camk2 silencing cells. Moreover, protein-protein interaction assays were used to study the interaction between CaMK1 and CaMK2. Besides, we also studied CaMK4. We studied whether PGAM5 is activated by CaMKs and thereby having effects to Drp1. In vivo, we confirmed the KN93 saves mice in transplantation and increases lengths survival time.Results. Mdivi1 and KN93 effectively prevented cell death. WB supported inhibitions of cell death had lower p-Drp1 expression. In addition, both CaMK1 and CaMK2 activate p-Drp1. Revolutionarily, we found CaMK2 is activated by either CaMK1 or CaMK4. p-CaMK4 escalated in CaMK1 silenicng cells. Moreover, CaMK2 interacts with PGAM5 during necroptosis.In vivo results supported KN93 lengths surival timeConclusions. CaMKs interactively activate each other and the down-stream PGAM5 and Drp1 to induce mitochondrial damage and necroptosis. Inhibition of CaMKs or Drp1 protects cell death and may be therapeutically used to prevent transplant rejection

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Michael MacNeil

A Case of Acquired Hemophilia A Masquerading as Anticoagulant-related Bleeding

Eman Mansory, Alejandro Lazo-Langner, Chai W. Phua

We report a case of a patient with recurrent hematomas while on anticoagulation for a pulmonary embolism and a prolonged hospital stay due to a delayed diagnosis for Acquired Hemophilia A (AHA). This case highlights the need for further awareness in AHA, potential laboratory pitfalls when conducting and interpreting coagulation assays, and the management considerations in a patient with a simultaneous thrombotic and hemorrhagic condition. We postulate that the lack of awareness of AHA promoted delay in diagnosis and the resultant prolonged hospital stay. A prolonged isolated activated partial thromboplastin time (aPTT) in a bleeding patient warrants workup for AHA.

Lorenzo Madrazo

"It's what we can do for now": Professional Identity Formation Among Internal Medicine Residents During the COVID-19 Pandemic

Grace Zhang, Kristen A. Bishop, Andrew Appleton, Mala Joneja, Mark Goldszmidt

Background: The COVID-19 pandemic has created unprecedented changes in how residents learn and provide patient care. Gaining insight into how these changes may be influencing professional identity formation can support programs as they seek to adapt training. Methods: We conducted semi-structured group interviews with 24 Ontario Internal Medicine (IM) residents in PGY 1-3 between November 2020 and July 2021. Participants were asked to reflect upon their experiences of learning and providing care during the pandemic. Constructivist grounded theory guided the iterative data collection and analyses. This process was further sensitized by Argyris and Schon's concepts of espoused theories and theories-in-use. Results: Participants consistently recognized the importance of collaboration and communication and developed several strategies for supporting patients and families affected by hospital restrictions. There was also a desire to advocate for disadvantaged patients facing barriers to accessing care. However, many felt powerless in their role as residents to enact meaningful change for their patients in the face of systemic constraints. In contrast, some felt empowered to be advocates when supported by their attending physicians.Conclusions: Residency training during the pandemic appears to have catalyzed the development of patient-centred competencies of communication and collaboration that are, in the literature, frequently identified as lacking in physicians. Concurrently, participants found it challenging to develop their roles as advocates in the face of systemic barriers. Programs should be mindful of these impacts to further support residents' development as advocates. Empowerment from attending physicians is important in fostering this aspect of their professional identity.

Hamza Mahmood

Retrospective Study of Delayed Renal Recovery in HELLP Syndrome

Cassie Fayowski, Susan Huang, Dongmei Sun

BackgroundHemolysis, elevated liver enzymes and thrombocytopenia (HELLP) syndrome is a severe, multi-system process occurring in 0.5-0.9% of pregnancies. Acute kidney injury (AKI) has previously been described to affect 7-25% of cases of HELLP syndrome in older series. The resulting complications from HELLP related AKI range from full renal recovery, to need for renal replacement therapy, to death. Other studies show a wide variance in prevalence of AKI in HELLP, and the expected course of recovery.It is unclear what the incidence and consequences of AKI in HELLP syndrome is in our institution. We sought to conduct a case series on patients at our institution with HELLP syndrome complicated by AKI.MethodsThis is a retrospective case series conducted at the London Health Sciences Centre and St. Joseph's Health Care London, on all pregnancies with a diagnosis of HELLP from January 2001 to October 2020. Potential participants were identified using ICD-10 codes for preeclampsia and HELLP syndrome both from admission diagnosis and discharge diagnosis. In addition, investigator's case files were used. Charts were screened by two independent physicians. Data abstraction from patients' hospital charts was done to identify cases as patients with HELLP syndrome with AKI, and then subdivided into rapid renal recovery (within 48 hours postpartum) or delayed renal recovery (beyond 48 hours postpartum). Descriptive statistics and graphs were used to describe the cohort.ResultsA total of 1862 charts were obtained for screening. Screening, data collection, and results are currently in progress.

Aminmohamed Manji

The role of aging on microvascular endothelial barrier function within the lungs

Sanjay Mehta, Lefeng Wang, Cynthia M. Pape, Sean E. Gill

Elderly individuals have an elevated risk of worsened outcomes and mortality under conditions of lung injury. Our lab has previously shown that lung injury is associated with damage to pulmonary microvascular endothelial cells. Endothelial cells interact with each other through cell-cell junctions to form a barrier between the lung tissue and the circulation. During lung injury, the endothelial barrier becomes damaged, causing fluid and protein leakage, and subsequent respiratory dysfunction. Pilot data from our lab showed increased leak within the lungs of aged mice with lung injury, compared to young mice. Furthermore, previous studies have demonstrated impaired endothelial cell function and cell-cell junction integrity with age. Based on this, we hypothesize that endothelial barrier function within the lungs declines with age, due to impaired cell-cell junction integrity. To address this, microvascular endothelial cells isolated from lungs of young and aged mice were cultured in vitro, until they formed a confluent monolayer.

We quantified macromolecular leak across these monolayers using Evans blue-labelled albumin and examined the integrity of the adherens junction protein, vascular endothelial (VE)-cadherin, through immunofluorescence microscopy. We found a 571% increase in leak in aged compared to young endothelial monolayers, which was associated with VE-cadherin disruption under basal conditions. We will next identify the mechanisms leading to impaired endothelial cell-cell junctions with age and how these mechanisms are implicated during lung injury. These findings may highlight the cellular pathways involved in predisposing aged individuals to worsened outcomes during lung injury, which can help in the development of therapeutics.

Leonardo Martin Calderon

Adult Onset Still's Disease: Points to Consider

Janet E. Pope

BackgroundAdult-onset Still's disease (AOSD) is a rare and complex autoinflammatory disease of unknown etiology. AOSD has varied presenting clinical features which can result in diagnostic uncertainty and prolonged time prior to treatment. ObjectiveTo review the literature and create a consensus on points to consider in the diagnosis, prognosis, and treatment of AOSD.MethodsA search of the AOSD literature over the last 15 years was performed on MEDLINE and EMBASE. Studies were included if they provided information regarding the epidemiology, diagnostic criteria, and treatment approaches in AOSD. Following narrative information synthesis a consensus on points to consider in AOSD was held. ResultsThe annual incidence and prevalence of AOSD is observed to be between 0.16 to 0.62 per 100,000 and 3.9 to 6.9 per 100,000, respectively. AOSD most commonly affects young adults and women. The Yamaguchi criteria remains the most widely used diagnostic tool with a sensitivity of 96.2% and specificity of 92.1%. Common presentation manifestations include intermittent high fevers (>39.0 degrees Celsius), arthralgias/arthritis, pharyngitis, lymphadenopathy, and a maculopapular rash. Common laboratory abnormalities include leukocytosis with neutrophilia, elevated ESR and CRP, elevated ferritin, and transaminitis. Initial treatment includes NSAIDs, glucocorticoids, and conventional DMARDs. Refractory disease is managed through IL-1 and IL-6 inhibitors. Elevated ESR, pericarditis, and nonresponse to corticosteroids are associated with refractory disease.ConclusionAOSD is a rare and multi-faceted autoinflammatory disease with a diverse presentation profile. Herein we provide points to consider in the diagnosis and management of AOSD following expert consensus.

Leonardo Martin Calderon

HIGHER RESOURCE UTILIZATION IN PATIENTS WITH SYSTEMIC SCLEROSIS COMPLICATED BY DIGITAL ULCERS

Tatiana Nevskaya, Murray Baron, Janet E. Pope

Background: Digital ulcers (DUs) occur in half of the patients with systemic sclerosis (SSc) and require healthcare interventions for treatment and monitoring for complications. Objective: We assessed the impact of DUs on resource utilization including hospitalizations, outpatient visits and procedures within a large SSc Canadian registry. Methods: 1698 SSc patients who completed one or more 84-item Resource Utilization Questionnaire (RUQ) for a 12-month recall period between September 2005 and February 2020 were included (9077 questionnaires). Organ involvement was assessed by disease severity scores on the Medsger scale. Unadjusted and adjusted regression analyses compared the association between DUs and resource utilization. Results: RUQs in 104 SSc patients with active DUs at two consecutive annual visits were compared with 104 patients without DUs matched 1:1 for age, sex, disease subtype and duration. Over one year, DUs were associated with higher number of tests ($p<0.05$) and visits to health professionals, especially to a rheumatologist ($p<0.0001$) and internist ($p=0.003$), a greater need for an accompanying person ($p<0.05$) and aids purchased/received ($p<0.05$). Having DUs was associated with more severe disease, even after excluding the peripheral vascular domain from a total DSS (9.7±4.5 vs 5.6±2.7, $p<0.0001$). After adjustment for disease severity in other organs, the presence of DUs remained a significant predictor of more frequent physician visits and more tests (all<0.05) by linear regression analysis.Conclusion: SSc patients with DUs utilized significantly more healthcare resources per annum even after adjustment for disease severity in other organ systems.

Leonardo Martin Calderon

Precursors to Systemic Sclerosis and Systemic Lupus Erythematosus: From Undifferentiated Connective Tissue Disease to the development of identifiable connective tissue diseases

Dr. Janet Pope

Background: The pathogenesis of connective tissue diseases (CTDs), such as systemic lupus erythematosus (SLE) and systemic sclerosis (SSc), is characterized by derangements of the innate and adaptive immune system, and inflammatory pathways leading to autoimmunity, chronic cytokine production, and chronic inflammation. The diagnosis of these diseases is based on meeting established criteria with symptoms, signs and autoantibodies. However, there are pre-clinical states where criteria are not fulfilled but biochemical and autoimmune derangements are present. Objectives:We aim to describe the role of the innate and adaptive immune system in the pre-clinical states

of UCTD-risk-SSc and prescleroderma, the underlying immune dysregulation in these pre-clinical states, and the evolution of antibodies from nonspecific antinuclear antibodies to specific prior to SLE development.Methods:We searched the databases EMBASE and MEDLINE with restrictions for the English language. Reference lists of all primary studies and review articles were searched for additional references.Results:Multiple cytokines are observed to increase along a disease spectrum from UCTD-risk-SSc to classified SSc and include sICAM-1, CCL2, CXCL8, ang-2, CXCL16, e-selectin, and IL-13. Furthermore, there are disease markers which are observed to be predictive of established SSc and include sIL-2Rα, PIIINP, CXCL4, CXCL10, and CXCL11. Pre-clinical SLE is characterized by an evolving IFN signature and progressive SLE-specific antibody formation prior to disease classification. Discussion:The coordinated dysregulation of the innate and adaptive immune systems, and inflammatory signaling pathways leads to the pathogenesis of CTDs. Our improved understanding of these underlying aberrations will serve to better identify patients at increased risk.

Muhtashim Mian

FEASIBILITY AND SEPTAL PERFORATION RATES IN LEFT BUNDLE BRANCH AREA PACING

Habib Rehman Khan, MBBS PhD

BackgroundLeft Bundle Branch area Pacing (LBBaP) is gaining prevalence as a more physiologic alternative to conventional right ventricular pacing. Given limited literature on LBBaP, this retrospective study assessed feasibility and septal perforation rates following LBBaP.MethodsProcedure reports and electrophysiologic parameters were reviewed of patients that underwent LBBaP since 2019. Partial septal perforation was defined as any two of: a) reduction of impedance by 200 ohms b) increase in capture threshold by 50% and c) decrease in ventricular sensing by 50% during follow-up compared to approximately 1-week post pacemaker implant.ResultsSince 2019, LBBaP was attempted in 168 patients and was successful in 102 (60.7 %), partial successful in 55 (32.7%) defined as QRS reduction of >20ms and duration <140ms, and unsuccessful in 11 (6.6%). QRS duration shortened or remained short after successful LBBaP compared to unsuccessful (113 vs 147 ms, $p < 0.001$). Left ventricular ejection fraction was similar following successful LBBaP ($p = 0.92$). Five patients (3%) had potential septal perforation based on above criteria. Lead revisions were not arranged for these patients as pacing requirements were not high and it was clinically appropriate to continue 3 monthly observations in clinic.ConclusionWe report success rates of LBBaP recently adopted in a large tertiary center. In a medium-term follow-up, we show that changes in electrophysiologic parameters likely consistent with partial septal perforation may occur spontaneously in some patients (3% in our cohort) over time.

Clinical significance of these changes and confirmation with imaging requires further study.

Gurjot Minhas

Beyond Budesonide - Treatment of Refractory Microscopic Colitis

My principal investigator was Dr. Nilesh Chande, who will be the last author as well.

AIM:Microscopic colitis is a clinical and pathological condition characterised by chronic watery, non-bloody diarrhoea, a normal or almost normal endoscopic appearance of the colon, and a distinct histologic pattern of collagenous or lymphocytic colitis. The diagnosis is made via endoscopically obtained biopsies of the right and left colon.Oral budesonide is widely accepted as the most effective treatment for patients with microscopic colitis based on clinical trials, and is used as therapy in most cases requiring prescription therapy, with a high response rate and low risk of adverse events. However, budesonide is not universally effective, and the ideal treatment for refractory patients is uncertain. The purpose of this paper is to review and summarize the literature evaluating treatments for microscopic colitis refractory to budesonide, and to determine their benefit in this patient population.Medline and Embase databases were utilized to search for primary literature. 1864 studies were screened, via their abstracts and full text when necessary. Patients included must have had histological diagnosis of microscopic colitis, and clinical failure of budesonide therapy budesonide therapy defined as ongoing symptoms despite budesonide.The age and sex of patients, whether they had collagenous versus lymphocytic colitis was included in each study was included where available. Clinical response characterised by an improvement in frequency of bowel movements was recorded and compared. Adverse events when available were highlighted

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Ahmed Mokhtar

Efficacy and safety of supraclavicular and pectoralis nerve blocks as primary peri-procedural analgesia for cardiac electronic device implantation: A Pilot Study

Pavel Antiperovitch MD FRCPC B(H)Sc, Raymond Yee, B.MD.Sc, MD FRCPC FHRS, Habib Rehman Khan MBBS PhD

Introduction: Cardiac implantable electronic devices (CIED) are routinely implanted using intravenous drugs for sedation. However, some patients are poor candidates for intravenous sedation. Objective: We present a case series that demonstrates the safety and efficacy of a novel, ultrasound-guided nerve block technique that allows for pre-pectoral CIED implantation in high-risk patients. The targets are the supraclavicular nerve (SCN) and pectoral nerve (PECs1). Methods: We enrolled 20 patients who were

planned for a new CIED implantation at LHSC. Following ultrasound guided-localization of the SCN and PECS1, LA was instilled at least 30-60 minutes pre-procedure. Successful nerve block was determined if less than 5ml local anesthetic was used interprocedurally, in addition to lack of sharp sensation with skin (SCN) and deep tissue pin-prick (PECS1). Results: The majority of patients (n=17, 85%) had successful periprocedural nerve block, with only 3 patients exceeding 5ml of LA. SCN and PECS1 success occurred in 19 (95%) and 18 (90%) patients, respectively. Only 8 patients (40%) received IV midazolam (mean dose 0.42mg, SD ± 0.63) and fentanyl (mean dose 12.5mcg, SD ± 19) With the exception of 1 patient, all patients reported a low Visual Analogue Score (0-2) immediately after, at 1 hr and 1 day post-procedure. There were no reported major adverse effects. Conclusion: SCN and PECS1 nerve blocks are safe and effective for patients undergoing CIED implantation to minimize or eliminate the use of intravenous sedation. A comparison study with the standard of care be will needed to assess the benefits of this technique.

Shara Nauth

Understanding how frailty is addressed in the training of perioperative specialists: A scoping review

Shara Nauth, Gabriella Jacob, Jenny Thain, and Jaspreet Bhangu

Background: There is an increasing need for frailty management in the perioperative setting. We aimed to identify and consolidate existing research on how frailty is addressed in relevant medical and surgical specialty training.Methods: We conducted a scoping review using the Joanna Briggs Institute framework. Three electronic databases (MEDLINE, EMBASE and Scopus) and the Cochrane library of systematic reviews were searched for articles published in January 1947 to April 2021. Abstract screening and full-text review were conducted by two reviewers. Data extraction was completed by the primary investigator.Results: Our search identified 3127 studies. 264 studies were reviewed at the full-text stage and 26 studies were included in the review. Three-quarters (n=20) were published in the last 5 years. All studies originated from a small number (n=5) of countries. Less than half (n=10) identified 'frailty' in the study objective. Studies included a range of perioperative specialties: surgical (n=18), anaesthesia (n=5), general medicine (n=4) or ICU (n=3). Most studies (n=21) assessed trainee knowledge (n=9) or perceptions (n=12) about frailty. Eight studies assessed the role of frailty in surgical decision-making. Of 8 studies involving an educational intervention, only one had frailty as the primary focus. The most commonly referenced frailty tool was the Clinical Frailty Scale (n=4).Discussion: This review identified a modest body of literature on how frailty is addressed in the training of perioperative specialists. Most studies examine knowledge and perceptions of perioperative trainees. Conclusion: Further investigation on the use of frailty educational interventions in perioperative training is needed.

Brent Parker

Effect of Levofloxacin Prophylaxis on Rates of Febrile Neutropenia in Patients Receiving DA-EPOCH-R Chemotherapy for Aggressive Lymphomas

Mina Dehghani, MD FRCPC; Selay Lam, MD FRCPC; Chai Phua, MD FRCPC; Cheryl Foster, MD FRCPC; Kang Howson-Jan, MD FRCPC; Joy Mangel, MD FRCPC

Introduction: The DA-EPOCH-R regimen is associated with high rates of febrile neutropenia (FN). This study examines the impact of adding routine Levofloxacin prophylaxis on FN and infection rates in patients with aggressive lymphomas receiving DA-EPOCH-R. Methods: This combined cohort study compares patients who received DA-EPOCH-R for newly diagnosed aggressive lymphoma at LRCP before and after the initiation of routine Levofloxacin prophylaxis in July 2020.Results: Thirty patients who received DA-EPOCH-R in the 5 years preceding the use of prophylactic Levofloxacin formed the retrospective cohort. Twenty-seven patients in the prospective cohort received Levofloxacin 500 mg for 7 days starting on day 8 of each cycle of DA-EPOCH-R, along with standard prophylactic Septra and G-CSF. Group demographics were similar: median age 58 (range 18-79) vs. 60 (range 19-78), male gender 66% vs. 70%, stage III/IV 90% vs. 67%. Cohort 1 received a total of 110 cycles of DA-EPOCH-R (median 4 cycles per patient, range 1-6) vs. 133 cycles (median 5 cycles per patient, range 1-6) in cohort 2. FN developed in 14 patients (47%) in the retrospective group, complicating a total of 20 chemotherapy cycles (18%). Three patients (11%) in the prospective group developed FN, complicating a total of 7 cycles (5%). There were 19 vs. 7 hospital admissions due to FN, and 2 vs. 0 deaths secondary to infection. No serious adverse effects from Levofloxacin were observed.Conclusions: The addition of routine Levofloxacin prophylaxis to DA-EPOCH-R was safe and effective, with significantly lower rates of FN, fewer hospitalizations, and no deaths secondary to infection.

Pavithra Parthasarathy

Assessment of Patient Education Resources in Myositis

Pari Basharat, MD

Background: Autoimmune myopathies (myositis) constitute a heterogenous group of illnesses characterized by systemic inflammation, notably with involvement of skeletal muscle. Along with the challenges that autoimmune myopathies pose for clinicians, their heterogeneity, complexity and rarity also pose challenges for patients. Currently, there is a dearth of comprehensive educational resources for patients living with myositis; while some resources exist, their quality and credibility has not been assessed. To date, there has been no systematic assessment of these resources, their credibility, and their efficacy in assisting patients with myositis. This project seeks to fill this gap.Methods: An online search of relevant keywords was used to form a list of relevant patient resources.

Resources from national/international organizations, as well as those affiliated with a known medical centre and/or university, were included to ensure a baseline degree of credibility. The Patient Education Materials Assessment Tool (PEMAT), a credible and reliable validation tool for patient resources, was used to perform a systematic assessment of these resources.Results: Currently in progress.Discussion: The results of this project will enable us to identify the utility and strength of these patient resources, and to help identify gaps in their offerings, as well as areas of improvement. With this information, we hope to help patients navigate these resources, by identifying which ones are most credible, scientific, and patient-friendly. As well, by analyzing the current resources and identifying gaps in their scope, we hope to help develop further robust, evidence-based resources for patients living with myositis.

Victor Pope

Safe utilization of ruxolitinib in simultaneous primary myelofibrosis and warm autoimmune hemolytic anemia

Cyrus Hsia

Primary myelofibrosis (PMF) is a myeloproliferative neoplasm that results in progressive fibrosis of bone marrow. Treatment for low-moderate risk disease is aimed at alleviating symptoms, and small molecules such as ruxolitinib, which inhibits JAK1/2, are newly available.Meanwhile warm autoimmune hemolytic anemia (wAIHA) is a condition where red blood cells are destroyed after being coated by IgG antibodies. It is associated with lymphoproliferative disease or infections and is treated with immunosuppression and therapy targeting the underlying cause.We report a case of a 58 year old woman with concurrent PMF and wAIHA successfully treated with ruxolitinib. She presented with jaundice, tea coloured urine, and progressive dyspnea. Her hemoglobin dropped to 57 g/L with evidence of hemolysis. Peripheral blood film demonstrated marked normocytic anemia with polychromasia, tear drop formation, spherocytes and circulating nucleated red cells. Her direct antibody test was positive for IgG and C3. Her bone marrow biopsy suggested an underlying myeloproliferative neoplasm. Next Generation Sequencing (NGS) revealed JAK2 and DNMT3A mutations, confirming PMF.Based on constitutional symptoms of nightly drenching sweats, anorexia, 20-pound weight loss and significant fatigue, she started ruxolitinib 20mg twice daily, alongside oral prednisone 1 mg/kg and folic acid daily for wAIHA.Since starting ruxolitinib, her symptoms improved, she regained weight, and her fatigue abated. Her wAIHA moved into remission during a 10 week prednisone taper. However, four months later, she showed signs of recurrent low-level hemolysis. With only ruxolitinib, her bone marrow is compensating, and her hemoglobin remains stable over two years without further immunosuppression.

Victor Pope

Outcomes In ANCA-Associated Vasculitis Patients with End-Stage Renal Disease - A Systematic Review and Meta-Analysis

Varunaavee Sivashanmugathas, Dirusha Moodley, Lakshman Gunaratnam, Lillian Barra

AbstractObjectivesPrior studies suggest that end-stage renal disease (ESRD) is associated with poor prognosis in patients with patients with anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This study summarizes the existing evidence for outcomes in AAV patients with ESRD.MethodsSearches of the MEDLINE and EMBASE databases were performed from inception until December 2021. Any study reporting outcomes after ESRD in patients with AAV were included. Mortality rate per 100 person-years (100py) calculated with a random-effects meta-analysis model was the primary outcome. Rates of infections, relapses, cardiovascular events, and malignancies were secondary outcomes.Results2470 citations were found; 23 studies of 1011 adult patients with over 3600 person-years of follow-up were included. The pooled mortality rate was 10.9 per 100py (95% CI: 7.11 - 14.7, I2 = 90.8%). The pooled infection rate was 66.6 infections per 100py (95% CI: 13.6 - 120, I2 = 99.6%). The pooled relapse was 6.22 relapses per 100py (95% CI: 4.64 - 7.80, I2 = 46.6%). Rates of experiencing at least one cardiovascular event or malignancy were 14.9 per 100py (95% CI: 12.4 - 17.4, I2 = 0.0%) or 2.37 per 100py (95% CI: 1.43 - 3.31, I2 = 0.0%) respectively.ConclusionsThere was significant heterogeneity among studies, but this analysis suggests AAV patients with ESRD have a lower risk of relapse, but higher infection and mortality rates. Infection and mortality risk was associated with exposure to cyclophosphamide. More prospective research and clinical trials exploring stopping immunosuppression after ESRD are needed

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Isabel Shamsudeen

The Intra-individual Temporal Variability of Lipoprotein(a)

Robert A. Hegele

Introduction: Lipoprotein(a) (Lp[a]) is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD). Lp(a) concentration is predominantly genetically determined, and has been suggested to remain stable over an individual's lifetime. The 2021 Canadian Cardiovascular Society dyslipidemia guidelines recommend measuring Lp(a) once in a patient's lifetime to assess ASCVD risk, given the assumption of biological stability, and because there is no current treatment to reduce Lp(a) nor evidence that reduction is beneficial. We evaluated stability in Lp(a) among lipid clinic patients assessed at multiple time points over >10 years of follow-up. Methods: A retrospective chart review of 12 patients from the University Hospital Lipid Genetics Clinic with multiple Lp(a) measurements was performed. Spearman's correlation

coefficient was used to determine intra-individual variability in Lp(a). Results: Median time between baseline and last follow-up Lp(a) measurements was 11.8 years (IQR: 9.7-14.0 years). Median Lp(a) was 99.1 mg/dL at baseline (IQR: 44.5-150.5 mg/dL) and 99.4 mg/dL at last follow-up (IQR: 70.6-110 mg/dL). Intra-individual Lp(a) values at baseline and follow-up were only moderately correlated (rho=0.45; p=0.15).Conclusion: While literature and guidelines imply temporal stability of Lp(a), our analysis demonstrates considerable intra-individual variability in Lp(a) over >10 years of follow-up, with absolute differences of up to 50% in the same individual at different time points. Larger-scale studies with longer-term follow-up could help inform future guidelines on the utility of single versus repeated Lp(a) measurements in ASCVD risk assessment.

Devanshi Shukla

Improving Patient Hand-Off On A Hematology Inpatient Unit

Derek NguyenMajid Gasim Sheikh MohamedDevanshi ShuklaAmara SimonMichael ShiDr. Uday Deotare

Handover is regarded as an important form of communication in transfer of care of patients between healthcare providers (HCP). The review of the handover process at London Health Sciences Centre (LHSC), in the Hematology Unit identified increased time and decreased efficiency related to communications during the handover process. Our aim was to improve the handover process with respect to time and make the process more efficient. A quality improvement (QI) project was conducted by six medical students and a HCP on the Inpatient Hematology Unit. Quantitative research approaches included a survey measuring overall satisfaction as well as measurements of handover time, cycle time, waste time and average takt time. Qualitative research approaches included interviews with members of the HCP team and assessing their satisfaction score. The QI team devised a new standardized approach to handover, by changing time of handover and introduction of a new format. Implementation of the newly created D2M-A2M format and change of handover from 1600 hrs to 0830 hrs reduced the average total handover time from 39 minutes to 29 minutes, while waste time decreased from 5.5 minutes to 1 minute. We found good acceptability but moderate adherence to the new format. Qualitative research showed lack of content standardization and inconvenient scheduling were key drivers of inefficient handover. Timely intervention and introduction of friendly format showed indicators of improvement. This project is in its 1st PDSA cycle phase. Further observation of cycles will elucidate the effectiveness of the new format. This project is still ongoing.

Robbie Sparrow

Readmissions after Left Atrial Appendage Closure in Patients with Previous Ischemic Cerebrovascular Accident

Luciano A. Sposato, Mohamad Alkhouli, Shubrandu S. Sanjoy, Adrian A. Kuchtaruk, Yun-Hee Choi, M. Chadi Alraies, Mamas A. Mamas, Rodrigo Bagur.

Objective: This study examined the frequency, causes and factors associated with 30- and 31-to-180-day readmissions after left atrial appendage closure (LAAC) in patients with and without a previous cerebrovascular accident (CVA).Methods: Hospitalizations for LAAC were identified from the United States National Readmission Database from January 1st, 2016 to December 31st, 2018. The primary outcome was first unplanned readmission after LAAC, with readmission times stratified into 0 to 30 and 31 to 180 days. Patients were stratified based on the presence of previous ischemic stroke or transient ischemic attack. Kaplan-Meier curves were used to assess whether previous CVA and post-LAAC in-hospital complications were associated with cumulative readmissions.Results: Among 12,901 hospitalizations, 5.2% of patients experienced an in-hospital complication, and 8.2% and 18% of eligible patients had a 30-day and 31-to-180-day readmission, respectively. The rate of in-hospital complications and readmissions during both time periods was not significantly different between CVA and non-CVA groups. Kaplan-Meier analysis did demonstrate a significantly higher cumulative readmission rate among patients with previous CVA at 11 months (P=0.03). Among patients with previous CVA, multivariable regression models demonstrated that heart failure, previous PCI, and anemia were the comorbidities that made the largest impact on 30-day readmission risk.Conclusion: The rate of 30-day and 31-to-180-day readmission after LAAC was similar between patients with and without previous CVA, but survival analysis did demonstrate significantly higher cumulative readmission rate among patients with previous CVA. Several patient factors and comorbidities were found to be independently associated with 30-day and 31-180-day readmissions.

Jordan Spradbrow

Thrombotic Thrombocytopenic Purpura Patients Have Evidence Of Global Longitudinal Myocardial Strain Up To One Year After Remission

Tanya Tamasi, Fabio Salerno, Kerri Gallo, Susan Huang

Introduction: Thrombotic thrombocytopenic purpura (TTP) is a potentially fatal thrombotic microangiopathy. Among TTP survivors, cardiovascular disease is the leading cause of death due to microvascular thrombi. Global longitudinal strain (GLS), assessed using 2D speckle tracking echocardiography can indicate subtle changes in myocardial mechanics, such as those induced by microvascular injury. These changes often precede structural changes visualized by traditional imaging. In this prospective observational study, we determined GLS of idiopathic TTP patients (iTTP) in

remission.Methods:Twenty-seven patients with iTTP were recruited between 2017-2021 within 3 days of admission to LHSC. Eligibility criteria included ADAMTS13 activity < 10% and detectable inhibitor at time of diagnosis. Echocardiography was performed at the start of remission (normalization of platelet count and LDH with no signs of microvascular injury for 30 days after last plasma exchange) and at 6 and 12 months after. Three consecutive heartbeats were analyzed for each image and the average strain of 12 left ventricular segments were used to calculate GLS. Longitudinal strain is represented by a negative value and values above -18% are considered abnormal (mean GLS in general population is -21%).Results:Eleven of 27 patient echocardiograms have been analyzed so far. The mean GLS at the start of remission was -15.7% (SD 3.5), at 6 months was -15.1% (SD 2.6) and 12 months was -15.5% (SD 1.9). Potential confounding clinical factors will be analyzed once echocardiogram analysis is complete.Conclusions:Patients in remission from iTTP have evidence of myocardial strain. They may benefit from longitudinal cardiology follow-up.

Munira Sultana

A novel phenotype of older adults with dual decline in gait and cognition at higher risk of dementia. A metabolomics analysis

Camicioli, R., Dixon, R., Faria, F., Petrotchenko, E., Speechley, M., Whitehead, S., and Montero Odasso, M

Introduction. We have shown that older adults presenting dual-decline in cognition and gait speed represent a phenotype of higher risk for dementia; a 6-fold risk when comparing with non-decliners. A biochemical characterization of metabolic perturbations in this novel group can assist in early identification of elevated dementia risk. We hypothesize that dual-decliners will have a unique metabolomic profile.Methods. Using the Gait&Brain Cohort (NCT03020381), we nested 19 participants from each of the following groups: pure-cognitive-decline, pure-motor-decline, dual-decline, no-decline, by matching them by age, sex and years of follow-up -3 years- (N=76). Cognitive and gait decline were operationalized as a decrease of ≥2 points in MoCA and reduction ≥10 cm/s in gait speed between baseline and the final assessment, respectively. We performed untargeted plasma metabolomics analysis across the 4 groups using Liquid Chromatography MS. Pair-wise comparison of detected compounds was done with Compound Discoverer, version: 3.2.0.421.Results. Principal components analysis and hierarchical clustering analysis did not detect any cluster separation in metabolomes across groups. However, 4 compounds were in significant higher concentration ($p< 0.05$) among the dual-decliners compared with non-decliner ($p< 0.05$, Fig 1). The cognitive decliner group had significant lower concentration of 7 compounds ($p< 0.05$) compared to the non-decliner group. Discussion: Dual-decliners at baseline present similar metabolomic profiles but with 4 compounds at higher concretions when compared with non-decliners. We elucidate these compounds and plan follow-up

metabolomics analyses of the groups. Results may point to pathways susceptible to treatments justifying a follow-up in the full sample (N=250).

Vivian Szeto

Successful treatment of Kimura Disease with Benralizumab

Benjamin Chin-Yee, Mina Dehghani, Kamilia Rizkalla, Christopher Licskai, and Cyrus C. Hsia

Kimura disease is a chronic inflammatory disorder that presents with lymphadenopathy and subcutaneous swelling in the otolaryngologic regions. A rise in IgE and peripheral blood eosinophilia are invariably present. Generally, Kimura disease affects young Asian males between the ages of 20 to 40 years old with the disease being more prevalent in Asia (Japan, China, Singapore, etc.). The pathophysiology of Kimura disease is poorly understood. However, there are findings supporting a type 1 and type 2 T cell mediated process based on the interplay between increased eosinophils, mast cells and the levels of IL-5 and IgE. The current treatment for Kimura disease includes systemic steroid therapy, immunosuppressive medications, and surgical resection.In this case report, we present a 41-year-old female with long standing asthma and Kimura disease with an elevated eosinophil count at 2.9 x 109/L and an otherwise normal complete blood count and white cell differential. She was initially treated with prednisone and upon tapering off had a relapse of her disease. She was then started on steroid sparing agents: cyclosporine and azathioprine without clinical benefit. She was subsequently approved for benralizumab, an IL-5 receptor inhibitor, and nine months into treatment has not had any recurrent of her symptoms. Her eosinophil levels are also undetectable. To our knowledge, this is the first case demonstrating the efficacy of benralizumab in treating Kimura disease.

Maria Tauqir

The Association between Vedolizumab and the Development of New-Onset Features of Spondyloarthritis in Patients with Inflammatory Bowel Disease: A Pilot Study.

Rohekhar, S., Boyd, T., Sharma, T., Khanna, R., Chande, N., Ponich, T., Gregor, J., Sey, M., Beaton, M., Mcintosh, K., Rahman, A., Jairath, V.

Background: Vedolizumab is a humanized IgG1 monoclonal antibody to α4Î²7 integrin approved for treatment of inflammatory bowel disease (IBD). Case series have suggested that vedolizumab may induce new-onset spondyloarthritis (SpA). However, it is unclear whether the arthritis developed after vedolizumab initiation, was present previously and under-investigated, or was masked by pre-existing therapy including tumour necrosis factor inhibitors (TNFi).Objective: To evaluate the association between

vedolizumab and development of new features of SpA in TNFi-experienced and TNFi-naive IBD patients.Methods: We performed a prospective observational study of 13 TNFi-naive and 11 TNFi- experienced IBD patients. Patients were assessed prior to vedolizumab initiation and 8 and 24 weeks after by a rheumatologist for historical and physical features of SpA, biochemical inflammatory markers, and clinical outcome measures for SpA and IBD. MRI of the sacroiliac joints was performed at each visit using a SpA protocol and centrally read by a blinded radiologist.Results: Twenty-four patients were recruited. One patient had evidence of burn-out sacroiliitis on MRI at baseline while another could not tolerate MRI; both were withdrawn. Five patients were lost to follow-up although one developed worsening joint pain and swelling after vedolizumab initiation. Sixteen of 17 patients (9 TNFi-naive, 8 TNFi-experienced) did not demonstrate new clinical or radiological signs of SpA. One TNF-experienced patient developed a worsening hip effusion at 24-weeks.Conclusions: The majority of patients treated with vedolizumab did not develop new manifestations of SpA which does not support the hypothesis that vedolizumab induces inflammatory arthritis. Larger studies are needed.

Daniel Taylor

A novel mechanism of Crohn's disease severity in women: evaluating the impact of an estrogen-farnesoid X receptor interaction on intestinal barrier function

Aze WilsonUte Schwarz

Crohn's Disease (CD) is an inflammatory intestinal disease with genetics and environmental factors contributing to its complex etiology. Recently, there has been growing appreciation for the potential protective role of the bile-acid sensing farnesoid X receptor (NR1H4, FXR) against dysregulation of the immune system seen in CD. Activation of FXR induces enteroprotective mechanisms including reduced production of both bile acids and proinflammatory cytokines. These effects serve to reduce epithelial permeability and inflammation of the intestines, both hallmarks of CD pathology.Recently, work by Wilson et.al. has suggested an association between the FXR single nucleotide variant (SNV) -1G>T (rs56163822) and risk of surgery in CD, specifically in female carriers. Previous in vitro research has shown that estrogen reduces expression of downstream FXR targets, notably the bile salt export protein (BSEP), so it is believed that females with a variant genotype are more likely to have reduced activation of other downstream FXR targets, including tight junction complex proteins. Through development of an FXR-1G>T-expressing colorectal adenocarcinoma (Caco-2) cell line, we will study the interaction between estrogen and variant FXR, specifically, the impact on FXR and tight junction protein expression in addition to tight junction integrity as assessed by cell monolayer permeability. We anticipate that interaction between FXR-1G>T and estrogen will result in reduced FXR and tight junction complex protein expression and increased cell monolayer permeability.

Additionally, the association between outcomes of severity in CD and estrogen exposure will be assessed in a large cohort of patients with CD.

Eric To

Quality Improvement Initiative to Optimize the Care of Patients with Sickle Cell Disease Presenting to the Emergency Department with Vaso-Occlusive Pain Crisis

Dr. Ziad Solh, Dr. Waseem El-Halabi

Background: Recently published guidelines recommend rapid assessment and multimodal management of vaso-occlusive crisis (VOC) in patients with sickle cell disease (SCD). Our hospital implemented an emergency department (ED) order set in 2019; however, impact on patient care outcomes has not been formally assessed. We are conducting a prospective quality improvement project to measure changes in outcomes over a 1-year period. Here we present baseline analysis.Methods: We used a combination of ICD-10 codes and our hemoglobinopathy clinic patient list to identify all instances of adult SCD patients presenting to the ED with VOC at two academic hospitals in London, Ontario, from January 1 to December 31, 2021. Our primary outcomes, adapted from the American Society of Hematology (ASH) Sickle Cell Disease quality metrics, were: proportion of patients who had a parenteral analgesic within 60 minutes of initial contact, and proportion of patients who had a pain assessment within 30 minutes following parenteral analgesic administration.Results: We identified 20 ED visits for VOC in 2021. Patients received parenteral analgesic within 60 minutes on 1 instance (5%). Eleven visits (55%) showed use of parenteral analgesia, and 6/11 (55%) had pain reassessment within 30 minutes of parenteral analgesia. Discussion: Local performance in rapid assessment and management of VOC crisis in the ED falls below the ASH quality metrics standard. We will conduct a prospective QI project to identify barriers to achieving this standard and design and implement a strategy to improve the ED care for patients with sickle cell disease presenting with VOC.

Jeffery Tong

Improving the efficiency of virtual insulin teaching for patients admitted to hospital through the COVID-19 pandemic

Sherrill Jackson, RN/CDE, St. Joseph's HospitalRebecca Meehan, RN/CDE, St Joseph's HospitalDane Iannicello, RN/CDE, St Joseph's HospitalUtbah Kazi, Schulich School of Medicine and DentistryRaymond Li, MD, Schulich School of Medicine and DentistryTisha Joy

Background: During the COVID-19 pandemic, many areas of medicine transitioned to virtual care to reduce viral transmission. For patients admitted to hospital, this included diabetes education (DE). Shifting to a virtual model for insulin teaching in particular, created new challenges for our inpatient DE team. Methods: We advanced a quality improvement project to improve the efficiency of virtual insulin teaching through the COVID-19 pandemic at London Health Sciences Centre. Our primary aim was to reduce the mean time between DE referral to successful inpatient insulin teach by 0.5 days. We implemented a new DE electronic order set that included a detailed referral request (PDSA-1). We added a streamlined method of insulin pen delivery to the ward for teaching (PDSA-2), followed by the inclusion of patient-care facilitators in the teaching process (PDSA-3). We captured the percentage of successful insulin teaches and readmissions to hospital as our balancing measure, and the percentage of successful insulin pen deliveries during virtual teaching as a process measure. Results: Between April 2020 and September 2021, the inpatient DE team completed 307 insulin teaches: 150 were in-person, 157 virtually. The average age of patients was 57-years (SD=16), 63% were male, and the majority (74%) had Type 2 Diabetes. Our tests of change improved the efficiency of virtual insulin teaching during the pandemic (run charts to be presented) without negative consequences. Conclusion: We improved the efficiency of virtual inpatient teaching at LHSC. However, in-person DE remained the most efficient way to successfully teach patients during hospitalization.

Jaspreet Toor

Immune Responses Against Citrulline and Homocitrulline in the Collagen-Induced Arthritis Mouse Model of Rheumatoid Arthritis

Sofya Ulanova, Garth Blackler, Ewa Cairns and Lillian Barra

Almost 1% of the world population suffers from rheumatoid arthritis (RA), a chronic autoimmune disease that causes pain, swelling and damage within synovial joints. RA has been characterized by autoimmune responses against post-translationally modified proteins, such as citrullinated proteins that have been extensively studied in RA. Up to 80% of patients express anti-citrullinated peptide autoantibodies (ACPA) and they have been shown to be pathogenic in RA models. In contrast, responses against proteins containing another post-translational modification known as homocitrullination are poorly understood, although >50% of RA patients produce anti-homocitrullinated peptide autoantibodies (AHCPAs). This study was conducted to investigate the relationship between immune responses to citrullinated and homocitrullinated proteins in the most commonly used mouse model for RA, collagen-induced arthritis (CIA). Male and female, 8-12-week-old, DBA/1J mice (N = 18) were immunized with type II collagen to induce arthritis. T cell recall responses were measured at sacrifice (day 50 post-immunization) using the CellTrace Violet proliferation assay. Serum collected every 14 days was tested for IgG ACPA and AHCPA by ELISA. Our preliminary results show, for

the first time, that T cell recall responses against homocitrullinated peptides develop in CIA mice. ACPAs and AHCPAs were also detected in CIA mice, similar to RA patients. This study helps characterize immune responses in the CIA mouse model to confirm its utility in future pre-clinical trials of RA-specific therapeutics.

Sofya Ulanova

Phenotyping of Homocitrulline-Specific T cells in Rheumatoid Arthritis

Ewa Cairns, Lillian Barra

Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterized by inflammation in the joints that affects 1% of the global population. The most significant genetic risk factor for RA is the human leukocyte antigen (HLA)-DR4 gene, which encodes for "Shared Epitope"• (SE), a five amino acid motif in the peptide-binding groove of Major Histocompatibility Complex (MHC) Class II molecules. Antigen-presenting cells expressing the SE can present citrullinated self-peptides to CD4+ T cells which leads to T cell activation, proliferation, pro-inflammatory cytokines release, and autoantibody production. It has been recently discovered that SE can also present homocitrullinated peptides. However, the phenotypes of T cells specific for novel homocitrullinated proteins remain unknown. In this study, we performed T cell phenotyping in DR4tg mice expressing SE in response to immunization with synthetic homocitrullinated peptide (HomoCitJED) developed by our laboratory. Male and female, 8-12-week-old, DR4tg mice (n=6) were immunized with HomoCitJED. Spleens were collected at different time points (10, 30, 70 days), and flow cytometry was performed to study T cell phenotypes. Our preliminary results show a greater proportion of activated, effector memory, T helper type 2 (Th2), and Th17 cells in HomoCitJED immunized mice compared to PBS controls. We believe that determining the phenotype of RA-specific T cells will help us understand immune responses to homocitrullinated antigens and will bring us one step closer to the development of antigen-specific therapy that can help RA patients live pain-free and high-quality lives.

Jeremy Vandelinde

Evaluation of the complication rates of renal biopsy in an inpatient and outpatient setting as it relates to 2-hour followup ultrasounds

Schorr M, Roshanov P, and A. House

Background: Previous studies of bleeding related complications of ultrasound-guided percutaneous renal biopsy have yielded a risk calculator (http://perioperativerisk.com/kbrc) and have led to the practice of 2-hour follow up ultrasound post biopsy.Study Design: We performed a retrospective analysis of 404 adult patients who underwent renal biopsy in an academic medicine centre in London,

Ontario between 2019 and 2021. We assessed frequency and timing of minor bleeding complications (not requiring intervention) and major (blood transfusion, IR embolization, surgery). We also collected patient data including BMI, Age, Sex, and lab values to validate the risk calculation previously developed.Results: Bleeding occurred in forty-eight of the inpatients (48/198, 24.2%) and seventy-two of the outpatients (72/206, 35.0%). Eight inpatient bleeding events required intervention (8/48, 16.7%), one of the outpatient bleeding events required interventions (1/71, 1.4%). Thirty-eight of the inpatient bleeding events were caught immediately post procedure (38/48, 79.2%), forty-nine of the outpatient bleeding events were caught immediately post procedure (49/72, 68.1%). Only one patient suffered a complication that required surgery or IR embolization. Further data regarding the validation of the risk calculator is forthcoming and will be included in the results along with the confidence intervals.Conclusions: Retrospective analysis of 404 patients receiving renal biopsy in the inpatient and outpatient setting demonstrated complication rates accurate to what was expected based on the risk calculations. These findings also support the practice of 2-hour follow up ultrasounds as a screening method for complications in the outpatient setting.

Logan VanNynatten

Next generation sequencing to determine etiology of renal disease: a prospective cohort study describing the Canadian experience

Dervla M. Connaughton M.D. MSc. PhD

Background:Recent data suggest that monogenic (single gene) diseases are underestimated in chronic kidney disease (CKD), particularly in adults with CKD of unknown etiology (CKDu). Retrospective studies show that 30% adult-onset CKD is monogenic. Prospective studies are needed to help guide integrating next-generation sequencing into clinical settings.Objective:Ongoing prospective, cohort-study to evaluate the diagnostic yield of next-generation sequencing testing in a Canadian clinic. The secondary objective is to determine the outcomes following establishment of a genetic diagnosis, to help guide physicians and policymakers on implementation of next-generation sequencing into clinical care. Methods:A targeted phenotype driven gene panel was performed if the subtype of CKD was evident at time of presentation. Exome sequencing was utilized for patients with non-diagnostic panels or in whom the subtype of CKD was unknown (i.e. CKDu).Results:To date, 95 families (138 individuals) have been recruited. We report on 43 families with CKD in whom next generation sequencing testing results are currently available. The median age of onset of CKD was 44 years (IQR 32-56). In 59% the subtype of CKD was unknown. A genetic diagnosis was confirmed in 42% of families. Exome sequencing yielded a genetic diagnosis in a further 10% who had a negative phenotype driven gene panel or had CKDu. Conclusion:This is the first study to prospectively characterize monogenic causation of CKD in a Canadian clinic setting. Genetic sequencing demonstrates a high prevalence

of genetic disease in CKD. Genetic sequencing informed prognosis and resolved diagnostic confusion in all cases.

DongYao(Donald) Wang

The role of CUB And Sushi Multiple Domains polymorphism as a genetic predictor of aromatase inhibitor induced arthralgia in post menopausal estrogen receptor positive breast cancer patients

Samantha Medwid, Adrienne E. Borrie and Richard Kim

Purpose: Aromatase inhibitors (AI) are the first line therapy for estrogen receptor positive (ER+ve) breast cancer in post-menopausal women. AI induced arthralgia (AIA) is a common side effect in up to 50% of the patients. Previous studies have demonstrated that pharmacogenetics play a role in inter-individual susceptibility to AIA. The purpose of this study was to evaluate the impact of a genetic variation in CUB And Sushi Multiple Domains (CSMD1) gene, a known tumor suppressor, as a predictor of AIA in a retrospective cohort of post-menopausal patients with ER+ve breast cancer.Methods: 196 patients were enrolled at initiation of AI therapy with letrozole/anastrozole. Patients completed two validated self-report questionnaires assessing arthralgia symptoms at baseline and at two and six months follow up. Germline DNA of all patients was genotyped for CSMD1 (rs6990851). Results werepo0p-[--0--0 analyzed in combination with previous genetic predictors associated with AIA, including CYP19A1. Results: At the six-months follow up appointment, patients with homozygous CSMD1 variant have decreased arthralgia symptoms (p=0.049). Furthermore, the combination of CSMD1 and CYP19A1 genotypes demonstrated significant effect on arthralgia symptoms (p=.036). Finally, regression analysis demonstrated that homozygous CSMD1 variant was associated with decreased risk of developing arthralgia or discontinuing therapy (p=0.045).Conclusion: CSMD1 (rs6990851) genetic variation appears to be a novel genetic predictor of decreased AIA in post-menopausal women with ER+ve breast cancer. This effect may be mediated through its interaction with CYP19A1, as CSMD1 was previously shown to regulate CYP19A1 expression, the key enzyme involved in estrogen biosynthesis.

Wei Wang

The Glucose Management Indicator (GMI) Derived from Intermittently Scanned Continuous Glucose Monitoring (isCGM) - A Real-World Study

Selina Liu, Charlotte McDonald

Background: The Glucose Management Indicator (GMI) is a continuous glucose monitoring (CGM) metric that estimates glycated hemoglobin (A1C). Previous studies have shown variable levels of discordance between calculated GMI and laboratory A1C.

Objective: To determine the real-world accuracy of GMI in predicting A1C in our clinic population.Methods: We conducted a retrospective chart review of type 1 and type 2 diabetes patients who use the Abbott Freestyle Libre Intermittently Scanned Continuous Glucose Monitoring (isCGM), treated between January 1, 2020, and March 1, 2021. We identified patients using clinic administrative records, with a final sample of 245 patients. We collected information on demographics, diabetes history, factors that could affect accuracy of A1C or Libre readings, bloodwork, and CGM data. We compared laboratory A1C to the corresponding GMI for 14-day periods ending on the date of bloodwork.Results: Only 46% of 14-day GMI were within 0.5% absolute value of A1C. This was minimally improved at 52% when potential interfering factors for A1C and Libre accuracy were excluded. Bland Altman analysis showed the 14-day GMI were, on average, 0.59% lower than A1C. Concordance between GMI and A1C improved when GMI was adjusted using the GMI and A1C difference from a previous date for the same patient.Discussion/Conclusion: GMI was not accurate in predicting A1C in about half of patients and underestimated A1C. The "gap"• between GMI and A1C may be stable within the same patient over time. Clinicians and patients should interpret the GMI with caution, in the absence of laboratory A1C.

Kathleen Winger

Pragmatic Evaluation of an Algorithm using D-dimer Adjusted to Clinical Probability in the Diagnosis of Pulmonary Embolism

Taylor Bechamp, Angela Wang, Lauren Chan3, Matthew D. Leeder, Christine MacDonald, Alejandro Lazo-Langner

BACKGROUND: Exclusion of pulmonary embolisms (PEs) using the Wells score and D-dimer < 500ng/mL (DD) is standard practice. The PEGeD study (Kearon et al. 2019) concluded that PEs can be excluded in patients with low clinical pre-test probability (C-PTP) and DD <1000ng/mL or moderate C-PTP and DD <500ng/mL. In this study we aimed to evaluate the PEGeD algorithm in daily practice.METHODS: We conducted a retrospective cohort study involving non-pregnant adult patients presenting to LHSC between November 2018 - December 2020 with symptoms of a PE with a DD ordered. Using the electronic hospital chart, we extracted data and applied the PEGeD algorithm. The outcome of interest was the proportion of PEs at 90 days post presentation in patients with a low or moderate C-PTP. RESULTS: A total of 2769 patient charts were reviewed. Of the 1070 included, 71 (7%) had a PE on initial presentation. At 90 days post presentation none (99% CI 0, 0.84) of the 787 patients with a low or moderate C-PTP score and DD <1000 or <500ng/mL, were positive for a PE. Notably, 8 (1.02%, 99% CI 0.42-2.43) PEs would have been missed.CONCLUSIONS: If the PEGeD algorithm was used, it would have resulted in a low risk of PEs during follow-up in patients with a low or moderate C-PTP. It was also associated with 194 (48%) less

diagnostic imaging studies in the low C-PTP and 2 (6%) less studies in the moderate C-PTP. Despite this, 1% of patients with PEs would have been missed.

Lauren Winquist

Subjective symptoms of orthostatic hypotension in older adults with cognitive impairment.

Laura Fitzgibbon-Collins, Shashankdhwaj Parihar, Michael Borrie, Jaspreet Bhangu

Background: In Canada, more than 500 000 individuals are currently living with dementia, and this number is estimated to increase dramatically by 2030. Previous research has demonstrated a correlation between decreased cerebral blood flow and cognitive impairment, however the identification of individuals experiencing cerebral hypoperfusion based on clinical assessment remains a challenge. Aims: Estimate the prevalence of orthostatic hypotension symptoms in older adults with cognitive impairment. Methods: Analysis of data from a prospective, observational trial in patients (N=87) with cognitive impairment who have been enrolled in The Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND), a longitudinal trial in older adults with cognitive impairment. Study participants completed five standardized questionnaires: the Center for Epidemiological Studies Depression Scale, the Orthostatic Hypotension Questionnaire, the Composite Autonomic Symptom Score, The Orthostatic Discriminant and Severity Scale, and the Mini Nutritional Assessment. Results: The prevalence and severity of orthostatic, autonomic, depressive, and malnutrition symptoms in older adults with cognitive impairment will be determined and analyzed. Conclusions: Future directions of this project will aim to correlate these symptoms with objective measurements of cerebral hypoperfusion to ultimately allow for the recognition of individuals with decreased cerebral blood flow at risk of worsening cognitive impairment.

Derek Wu

The accurate determination of lung sliding on lung ultrasonography using a deep learning approach

Blake VanBerlo BESc, Brian Li, Bennett VanBerlo, Marwan A Rahman, Gregory Hogg, Jared Tschirhart MSc, Alex Ford BSc, Jordan Ho MD, Joseph McCauley, Benjamin Wu BSc, Jason Deglint PhD, Rushil Chaudhary MD, Chintan Dave MD, Robert Arntfield MD

BACKGROUND: Pneumothorax is a potentially life-threatening condition that can be reliably diagnosed with high accuracy at the bedside using lung ultrasound (LUS). On LUS videos, the shimmering of pleura, termed 'lung sliding', rules out pneumothorax at the location of the ultrasound probe. The absence of lung sliding is concerning for a pneumothorax. On LUS M-mode images the seashore and barcode sign are cardinal

patterns associated with the presence and absence of lung sliding, respectively. Image classification using deep learning methods have been used to predict certain diseases with several imaging modalities, including LUS. OBJECTIVES: To develop (1) a preprocessing method that derives an M-mode image from LUS video clips and (2) a deep learning binary image classifier to predict the presence or absence of lung sliding on resultant M-mode images. METHODS: An object detection model was built to sample the pleural line on LUS clips where the M-mode images were derived. A binary classification model using the EfficientNetB0 architecture was trained using 2038 LUS clips from 832 patients with M-mode images as inputs. Grad-CAM was used as an explainability method to generate heatmaps providing insight on important features learned by the classification model on M-mode images. RESULTS: Our binary classifier was able to predict the absence of lung sliding with a sensitivity of 93.5%, accuracy of 88.9%, specificity of 87.3%, and AUC of 0.973. Grad-CAM visualizations confirmed the model's attention to relevant regions on M-mode images.

Laura Xu

Acidic pH Environment Alters Necroptosis and Regulates AIF Translocation in Endothelial Cells

Patrick McLeod, Xuyan Huang, Zhu-Xu Zhang

Introduction: Necroptosis is a caspase-independent death modality where organelle swelling, plasma membrane rupture, cell lysis, and leakage of intracellular components leads to secondary inflammation. It is a therapeutic target in ischemia-reperfusion injury, where an acidic microenvironment can affect transplant success. Apoptosis-inducing factor (AIF) is implicated in caspase-independent cell death and DNA damage following nuclear translocation. However, its role in acidic conditions has not been established.Methods: Mice microvascular endothelial cells (MVECs) were isolated. Cell death was quantified by real-time imaging using media adjusted to pH 7.4, 6.5, 6.3, and 6.0 and treated with combinations of TNF-α [T], second mitochondrial activator of caspase [S], IETD [S], and necrostatin-1s [N]. Immunochemistry staining for AIF was performed and nuclear translocation was quantified using fluorescent images. Nuclear fragmentation was measured and visualized by agarose gel. MVECs transfected with siRNA targeting AIF was confirmed with qPCR and western blots.Results: The TS and TSI groups at pH 7.4 had the highest levels of cell death, inducing apoptosis and necroptosis respectively. At acidic pH, TSI was protective against cell death, suggesting that the mechanism of necroptosis is altered. Nuclear translocation of AIF increased at acidic pH in all treatment groups and DNA laddering was present at pH 6.5.Discussion: Prolonged ischemia during cardiac transplantation due to the cessation of blood flow induces anaerobic metabolism, lactic acid accumulation, and intracellular acidosis. Understanding the mechanisms underlying ischemia and the acidification of the cellular

environment may improve cardiac transplantation success.Keywords: endothelial cells, apoptosis-inducing factor, necroptosis, apoptosis

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Joint pain and functional impairment in patient with acromegaly.

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BACKGROUND: Acromegaly can be associated with joint disease that can persist despite biochemical disease control and can have profound effects on quality of life. OBJECTIVES: To determine the burden of symptoms and impact on joint function in patients with acromegaly (ACRO) compared to those with non-functioning pituitary adenomas (NFPA). METHOD: A cross-sectional study consisting of ACRO and NFPA patients. Participants completed a series of standardized surveys and tools which asses physical function in the upper extremity (QuickDASH), stiffness, pain, and functional impact on the hip (HOOS-Jr) and knee joints (KOOS-Jr), and balance (ABC-6) in those with joint disease. Chi-square test and student t-test were used for statistical analysis. RESULTS: There was no difference between ACRO (n=42) and NFPA (n=38) for mean age (60.83+/-14.01 vs 59.87+/-10.81 year), BMI (31.10+/-6.43 vs 29.82+/-5.9 kg/m2), and gender (female 48% vs 50%). More ACRO patients underwent joint surgery than NFA patients (55% vs 25%, p=0.005), and more ACRO patients used pain medications (65% vs 40%, p=0.03). ACRO patients had greater impairment in upper extremity function (25.5+/-20.05 vs 12.56+/-12.52, p=0.001), hip function (69.52+/-20.16 vs 87.25+/-16.07, p<0.01), knee function (66.67+/-20.94 vs 81.17+/-19.23, p=0.002), and balance confidence (63+/-31% vs 70+/-22%, p<0.01). CONCLUSION: Compared to NFPA controls, ACRO patients more frequently report impaired functionality due to their joint disease, use more pain medication and are more likely to have had joint surgery. Prevention and management of acromegaly related arthropathy requires more attention in research and clinical practice.

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The Burden of Vascular Risks On White Matter Integrity And Cognition In Dementia

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BackgroundWhite matter abnormalities are frequently observed on MRI of the aging brain and is associated with cognitive impairment . We aimed to determine if vascular risk factors measured longitudinally would impact white matter integrity in older adults with cognitive impairment.MethodIndividuals between ages 60 and 90 with a confirmed diagnosis of dementia. Demographic, cognitive and lifetime vascular risk factor history was obtained at enrollment. 3T MRI imaging using standard sequences were acquired

at the time of enrollment and reviewed by two trained, blinded experts for white matter hyperintensity (WMHi). Between-group comparisons, two-sided t-tests and analysis univariate analyses of covariate (ANCOVAs)were used. Binomial logistic regression was used to assess whether vascular risk factors could predict high vs. low burden of WMHi. Results156 subjects were analyzed. Subjects with high burden WMHi had a significantly higher age compared to those with low burden WMHi (77.00 [SD: 6.43] vs. 71.65 [SD: 7.16], $p<0.001$). MoCA scores between the low burden WMHi group were higher than high burden WMHi group (23.60 [SD: 4.19] vs. 22.15 [SD: 4.37], respectively) but this was not significant ($p = 0.942$). Age and vascular risk factors demonstrated an association with white matter hyperintensity ($\chi 2= 21.690$, $p=0.001$), but none of the vascular risk factors individually contributed to the model. ConclusionThe current study suggests that cumulative vascular risk factors are associated with white matter burden in individuals with dementia, and that age remains a significant factor contributing to white matter abnormalities in neurodegeneration.
