UNIVERSITY OF ALBERTA

DEPARTMENT OF MEDICINE
FACULTY OF MEDICINE & DENTISTRY

ME2 MAJUMDAR RESEARCH & QUALITY IMPROVEMENT DAY

& QI DAY

MAY 16, 2024. 08:00 AM

NARMIN KASSAM

Chair, Department of Medicine

Welcome, everyone, to the highly anticipated 2024 Me2 Majumdar Research and Quality Improvement Day! It is with great pleasure and excitement that we celebrate the intersection of research excellence and clinical quality improvement within the Department of Medicine and the Edmonton Zone Medicine Quality Council, Strategic Clinical Improvement Committee (SCIC).

Today marks a pivotal moment in our academic calendar, as we come together to honour the dedication, innovation, and accomplishments of our esteemed colleagues and trainees. This collaborative event serves as a testament to our unwavering commitment to advancing healthcare through evidence-based practices and continuous improvement.

Thank you to our distinguished speakers who will be guiding us through this day of exploration and enlightenment. First, we have Dr. Peter Liu, Chief Scientific Officer and Vice President of Research at the University of Ottawa Heart Institute. Dr. Liu's pioneering work in cardiovascular research and his visionary leadership make him an invaluable asset to our event.

Also joining us is Dr. Anshula Ambasta. Dr. Ambasta is an esteemed Assistant Professor at the University of British Columbia specializing in clinical effectiveness and evidence-based strategies. Dr. Ambasta's research on over-utilization of laboratory tests garnered substantial funding and recognition. She leads efforts to reduce low-value diagnostics and therapeutic services within health systems. Her expertise in clinical effectiveness and evidence-based strategies makes her an excellent addition to our lineup.

Together, Dr. Liu and Dr. Ambasta will share their expertise, insights, and vision for the future of research and quality improvement.

Let’s celebrate the achievements of our trainees, learn from our distinguished speakers, and reaffirm our commitment to excellence in research and quality improvement. Thank you all for joining us, at our 2024 Me2 Majumdar Research and Quality Improvement Day!

Narmin Kassam
Professor and Chair, Department of Medicine
Clinical Head, Medicine, Edmonton Zone

TABLE OF CONTENTS

PETER LIU

Keynote Speaker

Chief Scientific Officer
Vice President of Research
University of Ottawa Heart Institute

Peter Liu is the Chief Scientific Officer and Vice President of Research at the University of Ottawa Heart Institute, and also Professor of Medicine at the University of Ottawa and University of Toronto. He was the former Scientific Director of the Institute of Circulatory and Respiratory Health at the Canadian Institutes of Health Research. He is also the co-lead of a new research program on Brain-Heart Interconnections, a $109 million new research program funded by the federal government.

Professor Liu's research focuses on the pathophysiology and clinical outcomes of heart failure from bench to bedside. He has published over 480 peer-reviewed articles in high impact journals, and received numerous awards in recognition of his research and scientific accomplishments.

Dr. Ambasta received her BSc. (2009) in Biological Sciences and her medical degree (2012), both from the University of Calgary.

She subsequently completed a 5-year residency program in General Internal Medicine at the University of Calgary, followed by a Masters in Public Health at the Harvard T.H. Chan School of Public Health with a focus on Clinical Effectiveness.

During her Master's program, Dr. Ambasta worked to describe and manage the problem of over-utilization of laboratory tests in hospitalized patients.

She began her clinical appointment with University of Calgary in 2017 where she complemented her clinical practice as a General Internal Medicine physician with ongoing research in healthcare quality and patient safety.

Her research work in the area of low-value laboratory testing was funded by Alberta Health Services, Choosing Wisely Alberta, Canadian Society of Internal Medicine, Alberta Health Services, and Canadian Institutes of Health Research. She began her academic appointment with University of British Columbia in 2022 as an Assistant Professor in the Department of Anesthesia, Pharmacology, and Therapeutics. She is a member of the Therapeutics Initiative where she is building a research program on reduction of low-value diagnostics and therapeutic services in health systems.

DR. ANSHULA AMBASTA

Keynote Speaker

Department of Anesthesia, Pharmacology and Therapeutic
University of British Columbia

ABOUT THE EZMQC - SCIC

Edmonton Zone Medicine Quality Council -
Strategic Clinical Improvement Committee

The University of Alberta Department of Medicine and Alberta Health Services Zone Medicine Program had overlapping strategic priorities to develop a strong clinical quality improvement agenda and improve outcomes for Medicine patients in the Edmonton Zone.

As a result, the Edmonton Zone Medicine Quality Council - Strategic Clinical Improvement Committee was formed in alignment with the DoM strategic plan and the AHS quality management framework supported by a DoM funded strategic clinical improvement consultant co-located with the AHS administrative lead for Edmonton Zone Medicine.

This council working closely with both academia and frontline care providers provides the platform for strategic quality improvement interventions to be developed, tested and shared with the Edmonton Zone Medicine divisions, hospital sites and community partners. Ensuring communication and collaboration as this pertains to the areas of clinical activity and clinical administration.

To serve as a resource for regular evaluation of clinical needs and priorities, initiatives and processes to build a dynamic cycle of continuous improvement in the in-patient and ambulatory patient experience.

ABOUT THE EZMQC - SCIC

Jennifer Woods is Executive Director of University of Alberta/ Stollery Emergency and the University of Alberta Hospital/EZ Medicine Programs.

As part of one of Canada's clinical research and teaching hospitals, her portfolio consists of approximately 259 medicine beds, 88 Emergency beds (Adults and Pediatrics) with a range of Medical services including pulmonary, nephrology, Inpatient TB, Haematology, Geriatrics, Geriatrics Neurology, Family Medicine and General Internal Medicine. She has strategic responsibility for medicine programs across the Edmonton zone.

The UAH/Stollery Emergency treats more than 115,000 patients annually. It is a quaternary, Level 1 trauma centre that serves as a major referral centre and hub for patients in the Edmonton Zone, northern Alberta (i.e., north of Red Deer), north-eastern British Columbia, north-western Saskatchewan, the Northwest Territories, and Nunavut.

Together we focus on patient flow, quality improvement and implementation of new evidenced based initiatives while ensuring our patients, families and staff have an exceptional experience.

Previous to this role Jennifer has held several leadership roles in the Edmonton Zone during her 24+ years in health care delivery. Her administrative leadership contributions include quality improvement, and implementation of patient and family-centered care initiatives. In addition to her passion for exceptional care and innovation, Jennifer enjoys spending time with her son and daughter, and the outdoors.

Pamela Mathura is an improvement leader/scientist and an assistant professor for the University of Alberta Department of Medicine and Alberta Health Services-Edmonton zone Medicine. Her role as a quality leader for the Edmonton zone medicine quality council-Strategic Clinical Improvement Committee includes leading quality improvement (QI) teams and providing foundational QI training. Pamela has published several articles in the area of improvement science and has a PhD in Healthcare Quality from Queens University.

Previous to this role Pamela has worked as a clinical quality improvement manager within Alberta Health Services. She has been involved in many large-multi-hospital QI projects which have been shared locally and provincially. Involved in healthcare delivery for the last 30 years; her clinical background is in Laboratory Medicine where she held a leadership role in Anatomical Pathology at the University of Alberta Hospital.

FACULTY MEMBERS

CARRIE YE
ASSOCIATE PROFESSOR
RHEUMATOLOGIST

Dr. Carrie Ye is a Rheumatologist at the Kaye Edmonton Clinic where she is the Medical Director of Rheumatology in Immuno-Oncology Clinic and the Multidisciplinary Bone Health Clinic. She is an Assistant Professor and early career researcher conducting epidemiology research in the field of bone and joint health in individuals with cancer. She has an interest and is developing expertise in the application of AI in health care.

ELLINA LYTVYAK
ASSISTANT PROFESSOR
PREVENTIVE MEDICINE

Dr. Ellina Lytvyak completed her medical school in Ukraine and obtained her PhD in Gastroenterology. She was awarded a Hubert Humphrey Fellowship, Fulbright Scholarship, by the United States Department of State, and completed it at Tulane University, New Orleans, USA. She also completed her Postdoctoral Fellowship with the University of Alberta. She is certified in Obesity Medicine by the American Board of Obesity Medicine and specializes in this area. Her special academic and clinical interests are in the prevention and management of obesity, steatotic liver disease, adiposity-associated chronic diseases, and their risk factors at the individual and population levels.

DOMINIC MUDIAYI
CLINICAL LECTURER
GENERAL INTERNAL MEDICINE

Dr. Dominic Mudiayi is a Clinical Lecturer and Consultant GIM physician at the University of Alberta Hospital. He is the Lead for Quality Improvement in the Division of GIM, and the QI Representative on the GIM Residency Program Committee. Dr. Mudiayi is also the GIM Liaison on the Edmonton Zone Medicine Quality Council, Strategic Clinical Improvement Committee. Recently, he completed a Master of Science in Healthcare Quality at Queens University. Dr. Mudiayi has led and been involved in numerous RQ and research projects including efforts to improve resident wellness, assessments of global health disparities in non-communicable diseases, equity in medical education and care pathways in clinical Medicine.

STEPHANIE SMITH
PROFESSOR
INFECTIOUS DISEASES

Dr. Smith is a professor at the University of Alberta in the division of Infectious Diseases. She is the Director of Infection Prevention and Control (IPAC) for the University of Alberta Hospital and the Mazankowski Heart Institute and the Medical Director of IPAC in the Edmonton Zone. She is a member of the Canadian Hospital Epidemiology Committee and co-chair of the Canadian Nosocomial Infection Surveillance Program (CNISP). Dr. Smith is also on a number of national and provincial guideline committees related to infection control practices to prevent the spread of antimicrobial resistant pathogens. She is a member of the PHAC Infection Prevention and Control Expert Working Group. Dr. Smith is involved in medical education at the undergraduate and postgraduate levels and served as the program director for the infectious diseases training program at the University of Alberta Hospital for nine years.

Program at a Glance

7:30 AM	Registration/ Refreshments
8:00 AM	Welcome Address
8:10 AM	Keynote Speaker *(Scientific)*
8:45 AM	Oral Presentations
9:35 AM	Break
9:45 AM	Oral Presentations
10:35 AM	Ballerman Translational Research Fellowship Award
10:55 AM	Faculty Presentations
11:00 AM	Poster Presentations
1:00 PM	Keynote Speaker *(Quality Improvement)*
1:35 PM	Oral Presentations
2:50 PM	Faculty Presentations
3:15 PM	Closing Address

Scientific Research Awards

SCIENTIFIC ORAL PRESENTATIONS AWARD WINNERS
$750

SCIENTIFIC POSTER ABSTRACT AWARD WINNERS
$500

PAUL MAN AWARD WINNER
$500

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD WINNER
$24,500

Abstracts have been adjudicated in a blinded fashion by 3 reviewers. The top 10 highest scoring abstracts in research and top 5 highest abstracts in quality improvement were invited to present an oral presentation

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

KARTHIVASHAN GOVINDARAJAN (2023)
SUPERVISOR: SATYABRATA KAR
Significance of native PLGA nanoparticles in the treatment of Alzheimer's disease pathology

GINA SYKES (2022)
SUPERVISOR: GLEN JICKLING
The aging immune system in acute ischemic stroke: A transcriptomic analysis

JOSEPH KAMTCHUM-TATUENE (2021)
SUPERVISOR: GLEN JICKLING
Prevalence of High-Risk Plaques and Risk of Stroke in Patients with Asympatomatic Carotid Stenosis: A Meta-analysis

ANDREW MASOUD (2020)
SUPERVISOR: ALLAN MURRAY
Apelin directs endothelial cell differentiation and vascular repair following immune-mediated injury

BRUNO SALEME (2019)
SUPERVISOR: GOPINATH SUTENDRA
Tissue-specific regulation of p53 by PKM2 is redox dependent and provides a therapeutic target for anthracycline-induced cardiotoxicity

MARYAM ABADI (2019)
SUPERVISOR: ALDO MONTANO-LOZA
Poor performance of psoas muscle index for identification of patients with higher waitlist mortality risk in cirrhosis

ABDUL KALAM AZAD (2018)
SUPERVISOR: ALLAN MURRAY
FGD5 Regulates VEGF Receptor-2 Coupling to PI3 Kinase and Receptor Recycling

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

PAST RECIPIENTS

RANIA SOUDY (2017)
SUPERVISOR: JACK JHAMANDAS
Cyclic AC253, a novel amylin receptor antagonist, improves cognitive deficits in a mouse model of Alzheimer's disease

ROXANNE PAULIN (2015)
SUPERVISOR: EVANGELOS MICHELAKIS
Sirtuin 3 Deficiency Is Associated with Inhibited Mitochondrial Function and Pulmonary Arterial Hypertension in Rodents and Humans

BRANDON MILLAN & HEEKAK PARK (2016)
SUPERVISOR: KAREN MADSEN
Fecal Microbial Transplants Reduce Antibiotic-Resistant Genes in Patients with Recurrent Clostrdium Difficile Infection

STACEY REINKE (2014)
SUPERVISOR: CHRIS POWER
Implementation of metabolomics strategies in multiple sclerosis

PETER DROMPARIS (2013)
SUPERVISOR: EVANGELOS MICHELAKIS
Pioglitazone reduces angiogenesis by altering mitochondrial function and reducing hypoxia inducible factor-1 activation

VAIBHAV PATEL (2012)
SUPERVISOR: GAVIN OUDIT
Loss of ACE2 Exacerbates Diabetic Cardiovascular Complications and Leads to Systolic and Vascular Dysfunction: A Critical Role of the Ang II/AT1 Receptor Axis

GOPINATH SUTENDRA (2011)
SUPERVISOR: EVANGELOS MICHELAKIS
Fatty Acid Oxidation and Malonyl-CoA Decarboxylase in the Vascular Remodeling of Pulmonary Hypertension

MSC IN MEDICINE WITH SPECIALIZATION IN TRANSLATIONAL MEDICINE

The Department of Medicine (DoM) has made **Translational Medicine (TM)** a top priority. TM facilitates the "translation" of molecular discoveries to actual patients and populations. It requires a different way of thinking at all stages of the journey from a discovery in an animal lab to the point that, following successful clinical trials, the government approves the discovered therapy for humans. TM is a critical component of **Precision Medicine**, a new discipline that aims for "custom-made" therapies for patients, as opposed to the traditional "one treatment fits all model". This is because in order to apply an optimal therapy to a patient, one needs to understand the molecular and genetic differences that distinguish all patients from one another. Precision Medicine is now a top priority for the FOMD.

The need: To optimize the development of new "precision" therapies and diagnostic tests, a researcher studying molecules and animals needs to learn how to think as a clinician; and a clinical researcher needs to understand the principles of molecular research. This is challenging because traditional teaching models focus on one or the other, with the learners following either an exclusive molecular or clinical research career track. Although all recognize the importance of TM, there are surprisingly few examples of training programs worldwide aiming to teach this new discipline to future medical researchers and leaders.

The action: Four years ago, the DoM launched and since then supports a novel training program, teaching the attitudes and skills required to excel in TM. This is the first training program of its kind in Canada and one of few in the world.

The innovations: The MSc in Medicine with specialization in translational medicine program attracts trainees from very diverse backgrounds and levels of training. Rather than teaching principles of basic or clinical research of specific diseases, the program teaches integrative and overarching concepts and skills to address the many challenges of bringing a molecular discovery to patients with diverse diseases. Since nothing needs to be "memorized", the final exams are "open book". Teaching objectives include, among others, new ways to design animal experiments or clinical trials compatible with PM, strategies to attract funding including grant writing skills, effective ways to communicate cross-disciplinary research findings, understanding of regulatory rules and "quality control" principles in preclinical and clinical research. Most of these principles are not taught in traditionally structured training programs. The trainees can either get credits towards their PhD or towards a novel Masters Program with "specialization in TM", the first of its kind in Canada.

The program uses eClass, the University of Alberta's centrally supported learning management system. eClass provides a digital platform in which the reading materials are archived as well as an out-of-class forum for ongoing discussions among trainees. All sessions are recorded through the eClass multimedia environment with Adobe Connect. This allows "live" streaming of sessions from other locations; thus the lectures can be attended interactively online by residents in a remote elective rotation or by trainees from other Universities. For example, in the last year 2 residents from UBC completed the program. The ability of residents to obtain a Masters degree during busy core Internal Medicine or specialty residency is a significant advantage to our clinical training programs.

The progress: A total of 109 learners have registered to the program so far. Of these, some took credits for their PhD and some participated as "open access" students. Of the 59 trainees that participated in the Masters track, there were 2 junior faculty members, 21 graduate students and 13 residents from core and 23 specialty residency programs. To complete the Masters requirements a submission of a thesis is required. So far 20 trainees have obtained their Master's with a specialization in TM degree.

The TM program is a major investment of the DOM, with many of its faculty contributing over the years. Currently, the program is directed by Evangelos Michelakis, MD, Gopinath Sutendra, PhD, Glen Jickling, MD, PhD and Eleni Karageorgos.

The MSc in Medicine with specialization in Translational Medicine class on April 19, 2018 (final exam day)

ORAL SCIENTIFIC PRESENTATIONS

7:30 AM **Registration/Refreshments**

8:00 AM **Welcome Remarks**
Dr. Narmin Kassam, Professor and Chair, Department of Medicine (DoM)
Dr. Evangelos Michelakis, Associate Chair (Research) Department of Medicine

8:10 AM **Keynote Speaker (Scientific Talk)**
Introductions by Dr. Evangelos Michelakis, Associate Chair, Research, DoM
Dr. Peter Liu, Professor, University of Ottawa and University of Toronto

ORAL SCIENTIFIC PRESENTATIONS

8:45 AM
Yongneng Zhang
Supervisor: Dr. Evangelos Michelakis
A critical contribution of cardiac myofibroblasts and a predictive role of UCP2 SNPs for right ventricular decompensation and CHF

8:55 AM
Ritu Mann-Nuttel
Supervisor: Dr. Paul Forsythe
Cultured human pulmonary neuroendocrine cells stimulated with house dust mite allergen activate innate lymphoid cells 2 and classic dendritic cells 1

9:05 AM
Jiyuan Piao
Supervisor: Dr. Evangelos Michelakis
A novel small molecule synthesized based on a snail hibernation model, induces hibernation in mouse fibroblasts and perfused hearts

9:15 AM
Hussain Syed
Supervisor: Dr. Andrew Mason
Transcriptomic Feature Importance Analysis for Treatment Response in Primary Biliary Cholangitis using Machine-Learning

9:25 AM
Maria Areli Lorenzana Carrillo
Supervisor: Dr. Gopinath Sutendra
Nuclear Versus Cytoplasmic/Mitochondrial TRIM35 Signalling in Cardiomyocytes may Predict Irreversible Versus Reversible Cardiac Dysfunction and Chemotherapy-Induced Cardiotoxicity

9:35 AM **Break**

ORAL SCIENTIFIC PRESENTATIONS

ORAL SCIENTIFIC PRESENTATIONS

9:45 AM
Saymon Tejay
Supervisor: Dr. Gopinath Sutendra
Tumour Secreted Inosine and Hypoxanthine Promote RBFOX1 Degradation, Cardiomyocyte Dedifferentiation and Susceptibility to Cardiotoxicity

9:55 AM
Luke Gagnon
Supervisor: Dr. Gavin Oudit
Uptake of SGLT2i and Outcomes in Patients with Diabetes and Heart Failure: A Population-Based Cohort and a Specialized Clinic Cohort

10:05 AM
Mustafa Al-Karaghouli
Supervisor: Dr. Juan G Abraldes
Relationship between updated MELD and prognosis in alcohol-associated hepatitis: opportunities for efficient trial design

10:15 AM
Narmeen Umar
Supervisor: Dr. Aldo Montano-Loza
Liver stiffness measurement by vibration-controlled transient elastography predicts adverse clinical outcomes in autoimmune hepatitis: results from a large multicentre longitudinal study

10:25 AM
Megan McCreary
Supervisor: Dr. Darren Lau
SGLT-2 Inhibitor Use in Adults (Age ≥ 65) with Diabetes and Cardiovascular Disease is Lower in Alberta and Manitoba than in Ontario: A Cross-Sectional Study

ORAL SCIENTIFIC PRESENTATIONS

BALLERMANN TRANSLATIONAL RESEARCH FELLOWSHIP AWARD

10:35 AM Ballermann Translational Research Fellowship Award Announcement

Oral Presentation

10:40 AM Ballermann Translational Research Fellowship Award Winner Presentation

FACULTY PRESENTATIONS

10:55 AM Dr. Carrie Ye - Faculty Oral Presentation

11:05 AM Dr. Ellina Lytvyak - Faculty Oral Presentation

11:00 AM Poster Presentations

ORAL QI PRESENTATIONS

1:05 PM **Keynote Speaker (Quality Improvement Talk)**
Dr. Anshula Ambasta
Department of Anesthesia, Pharmacology and Therapeutic
University of British Columbia

Oral QI Presentations

1:35 PM Shamaila Dar
Supervisor: Dr. Saifal Anwar
A Nocturnist Model Quality Improvement Project to Improve Patient Care and Overnight Support for Learners

1:50 PM Scott MacKay
Supervisor: Dr. Brendan Halloran
Assessing the Effectiveness of an Outreach Protocol for Biologic Naïve Ulcerative Colitis Patients – Ulcerative Colitis Clinical Outreach (UCCO)

2:05 PM Kyle Moxham
Supervisor: Dr. Darren Lau
Optimizing Point-of-Care Glucose Chemstrip Utilization in Hospitalized Patients: A Quality Improvement Initiative

2:20 PM Samina Khan
Supervisor: Dr. Gurpal Sandha
A quality assessment of the use of computerized tomography in the emergency department for patients diagnosed with acute pancreatitis

2:35 PM Victoria DeVito
Supervisor: Dr. Cynthia Wu
Use of the 4Ts Score in patients tested for HIT in our large academic centre

Faculty Presentations

2:50 PM Dr. Dominic Mudiayi, Clinical Lecturer, Division of General Internal Medicine, Department of Medicine

3:02 PM Dr. Stephanie Smith, Professor, Division of Infectious Diseases, Department of Medicine

3:14 PM **Awards Ceremony & Closing Remarks**
Dr. Narmin Kassam, Professor and Chair, Department of Medicine

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Albino, Larissa (Resident)
Case report: Steatotic liver disease diagnosed in a 24-year-old female with Rett Syndrome
Supervisor: Dr. Carlos Moctezuma Velázquez (Gastroenterology)

Aliy, Jokha (Graduate Student)
Redefininng the pathophysiology of spontaneous bacterial peritonitis in liver cirrhosis. The role of intracellular bacteria
Supervisor: Dr. Carlos Cervera (Infectious Diseases)

Al-Karaghouli, Mustafa (Resident (PGY3))
Prophylactic antibiotics in patients with alcohol-associated hepatitis receiving corticosteroids: A systematic review and meta-analysis
Supervisor: Dr. Juan G Abraldes (Gastroenterology)

Al-Karaghouli, Mustafa (Resident (PGY3))
Relationship between updated MELD and prognosis in alcohol-associated hepatitis: opportunities for efficient trial design
Supervisor: Dr. Juan G Abraldes (Gastroenterology)

Armbruster, Marie (Graduate Student)
Limited nesting in mice as a model to study the psychoneuroimmunology of post-partum depression.
Supervisor: Dr. Paul Forsythe (Pulmonary Medicine)

Beghin, Justine (Graduate Student)
An aptameric approach to interfering with Influenza's cap-snatching viral polymerase
Supervisor: Dr. Vanessa Meier-Stephenson (Infectious Diseases)

Bhangoo, Gurpriya (Graduate Student)
Monitoring of Remote Ischemic Conditioning with an Adjunct Tissue Reflectance Sensor in Patients with Acute Ischemic Stroke and Small Vessel Disease: A randomized Control Trial
Supervisor: Dr. Mahesh Kate (Neurology)

Bohlouli, Solmaz (Graduate Student)
Identifying guideline-concordant care after a severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in Alberta
Supervisor: Dr. Scott Klarenbach (Nephrology)

Charlton, Maddison (Graduate Student)
Correlating biophysical properties of TDP-43 aggregates with clinical phenotypes in amyotrophic lateral sclerosis and limbic-predominant age-dependent TDP43 encephalopathy
Supervisor: Dr. Valerie Sim (Neurology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Cooper, Matthew (Resident)
Trends in the burden of ischemic heart disease among patients with chronic kidney disease in Alberta
Supervisor: Dr. Aminu Bello (Nephrology)

Dembele, Kléouforo-Paul (Postdoctoral Fellow)
Nanotubes mediated mitochondria transfer from normal to cancer cells promotes Mesenchymal-to-Epithelial Transition (MET) needed for the establishment of metastasis in cancer
Supervisor: Dr. Evangelos Michelakis (Cardiology)

Duchesne, Marc (Graduate Student)
TSLP Secretion from Allergen-Treated Airway Epithelial Cells: Functional Role for Recycling Endosome Rab11a
Supervisor: Paige Lacy (Pulmonary Medicine)

Gagnon, Luke (Senior Subspecialty Resident R5)
Uptake of SGLT2i and Outcomes in Patients with Diabetes and Heart Failure: A Population-Based Cohort and a Specialized Clinic Cohort
Supervisor: Dr. Gavin Oudit (Cardiology)

Hindi, Mathew (Resident)
Outcomes Following Surgical Repair of Sinus Venosus Atrial Septal Defects: A retrospective study
Supervisor: Dr. Anoop Mathew (Cardiology)

Karamzadeh, Zahra (Graduate Student)
The contribution of skin in neuromodulatory effects through transcutaneous spinal cord stimulation
Supervisor: Dr. Vivian Mushahwar (Physical Medicine & Rehabilitation)

Kaviani, Rojin (Senior Subspecialty Resident R5)
Prevalence of metabolic-associated steatotic liver disease (MASLD) and its impact on adverse liver outcomes in patients with primary biliary cholangitis (PBC)
Supervisor: Dr. Ellina Lytvyak (General Internal Medicine)

Kaviani, Rojin (Senior Subspecialty Resident R5)
Impact of Sirolimus Proteinuria Following Liver Transplantation
Supervisor: Dr. Rahima Bhanji (Gastroenterology)

Khan, Lamia (Graduate Student)
Double-Stranded DNA Breaks, FOXO1, and polysialylation define a novel therapeutic axis in diffuse systemic sclerosis (SSc)
Supervisor: Dr. Mohammed Osman (Rheumatology)

Koerber, Daniel (Resident)
Variation in risk-adjusted cardiac intensive care unit (CICU) length of stay and the association with in-hospital mortality: An analysis from the Critical Care Cardiology Trials Network (CCCTN) registry
Supervisor: Dr. Sean Van Diepen (Cardiology)

Labib, Kirollos (Senior Subspecialty Resident)
Xanthogranulomatous Cholangitis: Rare, Benign Condition Mimicking Metastatic Cholangiocarcinomas
Supervisor: Dr. Kirles Bishay (Gastroenterology)

Lorenzana Carrillo, Maria Areli (Graduate Student)
Nuclear Versus Cytoplasmic/Mitochondrial TRIM35 Signalling in Cardiomyocytes may Predict Irreversible Versus Reversible Cardiac Dysfunction and Chemotherapy-Induced Cardiotoxicity
Supervisor: Gopinath Sutendra (Cardiology)

MacKay, Scott (Resident)
Peritoneal Dialysis-related Listeria monocytogenes Peritonitis Treated with Both Intravenous and Intraperitoneal Ampicillin – A Case Report and Literature Review
Supervisor: Dr. Mark McIsaac (Nephrology)

MacKay, Scott (Resident)
Comparing the Accuracy of Computed Tomography Enterography to Balloon Assisted Enteroscopy in the Evaluation of Small Bowel Crohn's Disease
Supervisor: Dr. Brendan Halloran (Gastroenterology)

Mandal, Shivani (Graduate Student)
The lung-brain axis: Insights from a Mouse Model of Chronic Allergic Airway Inflammation
Supervisor: Dr. Paul Forsythe (Pulmonary Medicine)

Mann, Darren (Graduate Student)
Examining the impacts of combining functional electrical stimulation assisted arm and leg cycling with epidural spinal cord stimulation after a motor complete spinal cord injury: A case study
Supervisor: Dr. Vivian Mushahwar (Physical Medicine & Rehabilitation)

Mann-Nuttel, Ritu (Postdoctoral Fellow)
Cultured human Pulmonary neuroendocrine cells stimulated with House dust mite allergen activate Innate lymphoid cells 2 and classic Dendritic cells 1
Supervisor: Dr. Paul Forsythe (Pulmonary Medicine)

Mansour, Juilian (Graduate Student)
A description of orientation and technological support strategies provided in Internet or mobile-based health interventions (IMIs) for adult patients.
Supervisor: Dr. Puneeta Tandon (Gastroenterology)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Marriott, Hazel (Graduate Student)
Thymic stromal lymphopoietin (TSLP) expression in nasal epithelial cells: Elevation in severe asthma
Supervisor: Paige Lacy (Pulmonary Medicine)

McCreary, Megan (Resident (PGY3))
SGLT-2 Inhibitor Use in Adults (Age ≥ 65) with Diabetes and Cardiovascular Disease is Lower in Alberta and Manitoba than in Ontario: A Cross-Sectional Study
Supervisors: Dr. Darren Lau (Gastroenterology)

Michaels, Margret (Graduate Student)
Variability in lung transplant clinical practices in Canada: Preliminary results of a national survey
Supervisor: Dr. Jason Weatherald (Pulmonary Medicine)

Michaels, Margret (Graduate Student)
Priorities for future lung transplant research: a preliminary report from a james lind alliance priority setting partnership
Supervisor: Dr. Jason Weatherald (Pulmonary Medicine)

Vivian, Nguyen (Clinical Fellow)
Immune checkpoint inhibitor liver-related adverse events: A Case Series
Supervisor: Dr. Aldo Montano-Losa (Gastroenterology)

Panesar, Simran (Graduate Student)
Development of a culturally appropriate, community-delivered management program for urinary incontinence in Sikh women – reflections on community engagement
Supervisor: Dr. Adrian Wagg (Geriatric Medicine)

Rahemtulla, Kahir (Resident (PGY3))
Impact of co-morbid Heart Failure on health outcomes following hospitalization for AECOPD
Supervisor: Dr. Mohit Bhutani (Pulmonary Medicine)

Sadasivan , Chandu (Resident (PGY2))
The role of early cardiac interventions in improving the clinical trajectories of patients with suspected genetic cardiomyopathies
Supervisor: Dr. Gavin Oudit (Cardiology)

Santos, Joy Ramielle (Graduate Student)
Identifying Patterns of Similarity between Upstream Gene Regions: Insights into Chromatin Organization and Gene Expression Across the Human Genome
Supervisor: Marcelo Marcet-Palacios (Endocrinology & Metabolism)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Sedaghat, Navid (Graduate Student)
Association between substance use and socioeconomic status using wastewater-based surveillance at eight neighborhoods in an urban center in Alberta, Canada
Supervisor: Dr. Monty Ghosh (General Internal Medicine)

Seyyedi, Noorossadat (Graduate Student)
p53 associated de novo activation of VWF expression in tumor cells
Supervisor: Dr. Nadia Jahroudi (Hematology)

Shah, Divya (Resident)
The Resilience of a Centralized, Public Health, Tuberculosis Program Performance in Alberta Before and During the Covid-19 Pandemic Disruption
Supervisor: Dr. Richard Long (Pulmonary Medicine)

Shelton, Jaclyn (Resident)
Predictors of Diagnostic Delays and Loss to Follow-up in Women with von Willebrand Disease
Supervisor: Dr. Hao Wei (Linda) Sun (Hematology)

Shreekumar, Devika (Graduate Student)
Sex, ethnicity and clinical outcomes in autoimmune hepatitis: results from a large multicenter longitudinal cohort
Supervisor: Dr. Ellina Lytvyak (Preventive Medicine)

Shyian, Melissa (Resident (PGY3))
Using a Shared Infusion Clinic for Outpatient Management of Sickle Cell Vaso-occlusive Crisis as a Strategy of Decreasing Emergency Department Visits
Supervisor: Dr. Lauren Bolster (Hematology)

Shysh, Andrea (Resident (PGY3))
New and persistent psychoactive medication use in intensive care unit survivors with COVID-19
Supervisor: Dr. Sean van Diepen (Cardiology)

Skoreyko, Jessica (Graduate Student)
Binding Hepatitis B virus' chronic form by targeting its pre-core promoter G-quadruplex
Supervisor: Dr. Vanessa Meier-Stephenson (Infectious Diseases)

SCIENTIFIC ABSTRACTS

FULL ABSTRACTS ENCLOSED

Syed, Hussain (Graduate Student)
Transcriptomic Feature Importance Analysis for Treatment Response in Primary Biliary Cholangitis using Machine-Learning
Supervisor: Dr. Andrew Mason (Gastroenterology)

Saymon, Tejay (Graduate Student)
Tumour Secreted Inosine and Hypoxanthine Promote RBFOX1 Degradation, Cardiomyocyte Dedifferentiation and Susceptibility to Cardiotoxicity
Supervisor: Gopinath Sutendra (Cardiology)

Umar, Narmeen (Resident (PGY1))
Liver stiffness measurement by vibration-controlled transient elastography predicts adverse clinical outcomes in autoimmune hepatitis: results from a large multicenter longitudinal study
Supervisor: Dr. Aldo Montano-Loza (Gastroenterology)

Wang, Kevin (Graduate Student)
Advanced Age Considerations in Randomized Clinical Trials of Adults Receiving Maintenance Dialysis: A Meta-Epidemiologic Study
Supervisor: Dr. David Collister (Nephrology)

Ye, Jeffery (Si Cong) (Resident (PGY3))
Validation of Emergency Medical Services Administrative Codes to Identify an Out-of-Hospital Cardiac Arrest Cohort
Supervisor: Dr. Sean van Diepen (Cardiology)

Zhang, Yongneng (Postdoctoral Fellow)
A critical contribution of cardiac myofibroblasts and a predictive role of UCP2 SNPs for right ventricular decompensation and CHF
Supervisor: Dr. Evangelos D. Michelakis (Cardiology)

QUALITY IMPROVMENT ABSTRACTS

FULL ABSTRACTS ENCLOSED

Bechard, Kaylin (Resident)
Improving Patient Outcomes in the Vulvar Dermatology Clinic
Supervisor: Dr Marlene Dytoc (Dermatology)

Cooper, Jared (Senior Subspecialty Resident)
Competency based medical education: o-score characteristics of procedural and cognitive assessments in gastroenterology residency training
Supervisor: Dr. Karen Kroeker (Gastroenterology)

Feng, Yuyang Julianne (Resident)
Patient directives to improve care for gestational diabetes: A systematic review of qualitative studies
Supervisor: Dr. Roseanne Yeung (Endocrinology & Metabolism)

Iqbal, Iffat (Resident)
Understanding Barriers to Referring Patients to a Deprescribing Clinic
Supervisor: Dr. Winnie Sia (General Internal Medicine)

Khan, Samina (Resident)
A quality assessment study to determine if tissue acquisition and specimen handling impact the diagnostic yield of endoscopic ultrasound-guided fine needle aspiration biopsy of solid mass lesions
Supervisor: Dr. Gurpal Sandha (Gastroenterology)

Liu, Crystal (Resident (PGY3))
Outcome of utilizing MELD 3.0 from a Canadian perspective: a retrospective study in a single tertiary-care transplant centre
Supervisor: Malcolm Wells (Gastroenterology)

Majumdar, Jasmin (Resident)
Understanding Provincial Ambulatory Patient Concerns and Commendation Data
Supervisor: Dr. Elaine Yacyshyn (Rheumatology)

Moxham, Kyle (Resident)
Optimizing Point-of-Care Glucose Chemstrip Utilization in Hospitalized Patients: A Quality Improvement Initiative
Supervisor: Dr. Darren Lau (General Internal Medicine)

Pascheto, Isabella (Resident)
What About Physician Wellness? Impact of a Quality Improvement Intervention
Supervisor: Dr. Narmin Kassam (General Internal Medicine)

QUALITY IMPROVMENT ABSTRACTS

FULL ABSTRACTS ENCLOSED

Patel, Kinjal (Senior Subspecialty Resident)
A quality assessment of the adequacy of fluid replacement therapy for patients diagnosed with acute pancreatitis
Supervisor: Dr. Gurpal Sandha (Gastroenterology)

Quan, Sophia (Senior Subspecialty Resident)
Advanced Hepatic Echinococcosis: A Case Report
Supervisor: Dr. Malcolm Wells (Gastroenterology)

Rasmuson, Jaslyn (Resident)
Active Mind, Active Body in Action: Assessing the Impact of Medical Student Volunteerism in the Hospital
Supervisor: Dr. Winnie Sia (General Internal Medicine)

Sage, Kayla (Resident)
Prescribing Improvement for the Prescription Refill Process
Supervisor: Dr. Elaine Yacyshyn (Rheumatology)

Wu, Allan (Resident)
Virtual Kidney Care during the COVID-19 Pandemic
Supervisor: Dr. Elena Qirjazi (Nephrology)

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Scientific Research Abstracts

CASE REPORT: STEATOTIC LIVER DISEASE DIAGNOSED IN A 24-YEAR-OLD FEMALE WITH RETT SYNDROME

Larissa Albino, Adil Adatia, Aducio Thiesen, Brendan Halloran, Victor Dong, and Carlos Moctezuma Velázquez.

Supervisor: Carlos Moctezuma Velázquez

INTRODUCTION

Rett syndrome (RTT) is a neurodevelopmental disorder in females that is caused by mutations to the methyl CpG binding protein-2 (MECP2) gene, characterized by developmental milestone regression and physical disability. This mutation contributes to disease burden by causing peripheral system perturbations, leading to dyslipidemia (DLD) and steatotic liver disease (SLD). Although DLD has been described in RTT patients, SLD has only been described in MECP2-null mice. This report presents a RTT patient who was diagnosed with SLD on liver biopsy in the context of DLD but without insulin resistance or other comorbidities associated with metabolic syndrome.

METHODS

Retrospective review of one patient.

RESULTS

A 24-year-old woman with RTT was seen at a tertiary care center for evaluation of abnormal liver enzymes (ALT 163, AST 51, ALP 258, total bilirubin 6). Abdominal ultrasound demonstrated moderately echogenic liver parenchyma consistent with steatosis. Transient elastography demonstrated a controlled attenuation parameter of 342 dB/m and stiffness of 7.1 kPa. Additional investigations were unremarkable. There was no history of alcohol misuse or new medications/supplements. Her homeostatic model assessment for insulin resistance score was 1.8, hemoglobin A1c was 4.8%, and lipid profile demonstrated DLD (elevated triglycerides, LDL). The decision was made to proceed with liver biopsy. This demonstrated moderate steatosis and no ballooning, categorized as grade A1, stage F1.

CONCLUSIONS

This report demonstrates RTT patients have similar lipid metabolism perturbations to those seen in MECP2-null mice, resulting in similar metabolic abnormalities such as DLD and SLD. The absence of insulin resistance and other comorbidities associated with metabolic syndrome further support these perturbations are caused by a pathophysiologic mechanism specific to RTT. This demonstrates the importance of screening RTT patients for DLD and SLD despite their young age to detect these conditions before complications arise. It also demonstrates MECP2-null mice can be used as models to identify future RTT therapies.

Redefininng the pathophysiology of spontaneous bacterial peritonitis in liver cirrhosis. The role of intracellular bacteria.

Jokha Aliy, Tanya Suandork, Aja Reiger, Carlos Cervera

Supervisor: Carlos Cervera

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is a severe complication of cirrhosis. SBP frequently recurs (probability of 43%, 69% and 74% at 6 months, 1 year and 2 years respectively), so secondary prophylaxis is required after a first episode. The accepted pathophysiology is infection of ascitic fluid through bacterial translocation from the gut. The aim of this study was to investigate the presence of intracellular bacteria in mesothelial cells of the peritoneum obtained from participants with ascites.

METHODS

We collected 300mL of ascitic fluid per participant and cells stored at -80 degrees. We investigated for presence of bacteria using scanning electron microscopy, imaging flow cytometry and confocal microscopy. Cells were fixed, blocked, permeabilized and stained targeting cell membrane, bacterial antigens and cell nucleus. Scanning electron microscopy (SEM) was used to visualize bacterial aggregates following cell lysis.

RESULTS

We included 10 participants. Free floating bacterial aggregates were identified by SEM in all participants, with a 7% nitrogen content of the extracellular matrix measured by energy dispersive X-ray by SEM, characteristics compatible with environmental microbiome. By ImageStream, an average of 2,486 cells and an overall prevalence of 45.66% cells were found to express intracellular bacterial antigens. While ImageStream could not finely characterize the intracellular signal, the spot size was too small to match intracellular bacterial aggregates. Confocal microscopy revealed all mesothelial cells observed expressed intracellular bacterial antigens. Using specific antibodies against Escherichia coli we identified structures compatible non-aggregated bacilli in 4/4 samples examined. However, we did not visualize in mesothelial cells, intracellular bacterial communities as described in urothelial cells.

CONCLUSIONS

The ascitic fluid microbiome is compartmentalized, with an extracellular component of environmental microbiome consisting of bacterial aggregates, and intracellular bacteria. The presence of E. coli suggests that intracellular bacterial reservoirs could explain both the occurrence and recurrence of SBP through mesothelial cell shedding into the ascitic fluid.

Prophylactic antibiotics in patients with alcohol-associated hepatitis receiving corticosteroids: A systematic review and meta-analysis

Joo Wei Ethan Quek, Jing Hong Loo, Aunchalee Jaroenlapnopparat, Cesar Jimenez, Mustafa Al-Karaghouli, Victor Vargas, Juan Pablo Arab, Juan G Abraldes, Yu Jun Wong

Supervisor: Juan G Abraldes

INTRODUCTION

The benefits of prophylactic antibiotics in patients with alcohol-associated hepatitis (AH) receiving steroids remain unclear. We aimed to assess the clinical impact of prophylactic antibiotics in AH patients receiving steroids.

METHODS

We systematically reviewed four electronic databases up to November 30, 2023. Pooled estimates were analyzed using random-effects models. The primary outcome was 90-days survival. Secondary outcomes included infection at days 30- and 90-days, hepatorenal syndrome (HRS), acute kidney injury (AKI), hepatic encephalopathy (HE), and drug-related adverse events (AE). Trial sequential analyses were performed for the primary outcome of 90-day mortality.

RESULTS

We screened 467 articles and included six eligible studies (four RCTs and two matched cohort studies) with a total of 510 patients. Compared to standard medical treatment (SMT), prophylactic antibiotics were associated with a lower risk of infection at 30-days (OR: 0.35, 95%CI: 0.20-0.59, I 2 =0%), infection at 90-days (OR: 0.25, 95%CI: 0.09-0.65, I 2 -0%), and a lower rate of HE (OR: 0.32, 95%CI: 0.12-0.87, I 2 =0%). However, prophylactic antibiotics did not improve 90-day survival, sepsis-related mortality, HRS, or AKI. The risks of drug-related AE and fungal infections were similar in patients with AH who received prophylactic antibiotics or SMT.
Using trial sequential analysis, the minimum sample size required to detect a 15% relative risk reduction in 90 days mortality with prophylactic antibiotics was 1,171.

CONCLUSIONS

In hospitalized AH patients receiving steroid therapy, prophylactic antibiotics reduced the risk of infection and HE, but did not improve survival or prevent AKI compared to SMT.

Relationship between updated MELD and prognosis in alcohol-associated hepatitis: opportunities for efficient trial design

Al-Karaghouli M, Ventura-Cots M, Wong YJ, Bataller R, Abraldes JG

Supervisor: Juan G Abraldes

INTRODUCTION

Alcohol-associated hepatitis (AH) is associated with significant mortality. MELD score is used to predict short-term mortality and aid in treatment decisions. MELD is frequently updated in the course of AH. However, once the most updated MELD is known, it is uncertain if previous ones still have prognostic value, which might be relevant for transplant allocation and trial design. We aimed at investigating the predictive performance of serial MELDs in patients with AH

METHODS

This is a prospective cohort of patients with AH by the InTeam consortium. 307 patients (with 859 MELD values within 60 days of admission) fulfilled the inclusion criteria. The main endpoint was time to death or transplant up to 90 days. We used a joint model approach to assess the predictive value of updated MELDs.

RESULTS

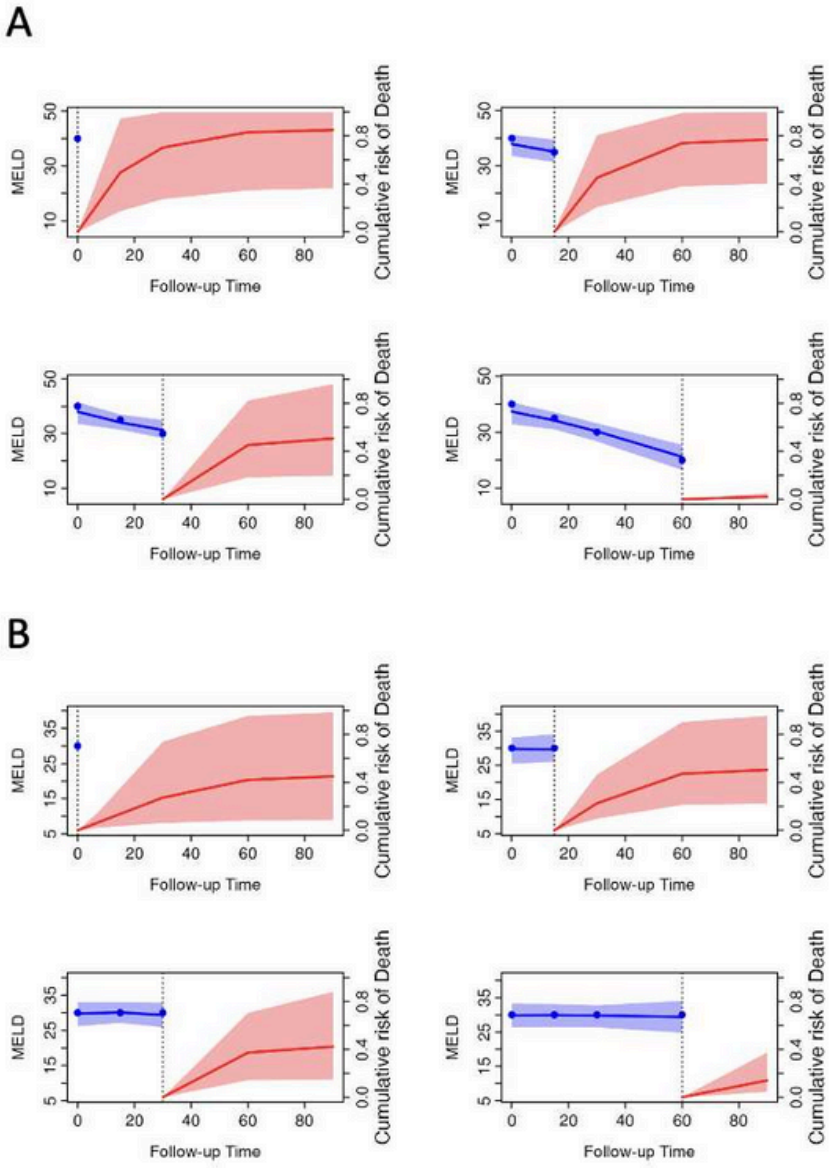
Results

Serial MELD measurement had a strong prognostic value for death/transplant (HR 1.20, 95% CI 1.14-1.27) ($p<0.0001$). Previous MELD values did not add predictive value to the most current MELD. We also showed that MELD at day 28 (MELD28) had a significant predictive value for subsequent mortality/transplant in a landmark analysis (HR 1.18, 95% CI 1.12-1.23). We show that the use of an ordinal scale including death, transplant and MELD28 as a trial outcome could substantially reduce the sample size required to demonstrate short term benefit of an intervention.

CONCLUSIONS

Conclusion

we show that updated MELDs during the trajectory of AH predict subsequent mortality or need for transplant. MELD28 inclusion in an ordinal outcome (together with death or transplant) could increase the efficiency of randomized controlled trials


A
MELD
Cumulative risk of Death
Follow-up Time
B
MELD
Cumulative risk of Death
Follow-up Time

Limited nesting in mice as a model to study the psychoneuroimmunology of post-partum depression.

Marie Armbruster, Paul Forsythe

Supervisor: Paul Forsythe

INTRODUCTION

Postpartum depression (PPD) is a common mood disorder that affects the ability of a mother to engage with and care for their infant. Stress exposure is a major predisposing factor for PPD, while immune factors are also hypothesized to influence development of this disorder. Here we assessed a limited nesting (LN) in mice as a potential model to investigate the relationship between stress and the immune system in PPD.

METHODS

Dams (C57BL6J) and their pups were provided limited nesting material from post-natal day 3-9 while controls had standard cages. Maternal behaviour was determined over the LN period followed by assessment of depressive-like behaviour using the splash test. Gene expression in selected brain regions and the immune profile of splenocytes was also characterized. For statistical analyses, t-test and ANOVA were used where appropriate.

RESULTS

LN exposure led to a significant increase in negative maternal behaviour ($p=0.007$, $n=11$) and a reduction in active nursing ($p=0.04$) but did not alter behaviour in the splash test. Regardless of postpartum environment, pregnancy was associated with an increase in the T regulatory cell population of the spleen compared to never pregnant age-matched females ($p<0.01$). Depletion of T regulatory cells with anti-CD25 antibodies resulted in lower maternal behaviour in response to LN that was associated with an increase in hypothalamic expression of oxytocin and its receptor (1.8 and 1.4 fold change) in addition to vasopressin and prolactin receptors (1.5 and 1.7 fold change).

CONCLUSIONS

A LN environment results in decreased maternal behaviours and increased negative behaviour towards pups but does not alter self-care behaviour. Our data also suggests that post-partum regulatory immune changes may mitigate effects of stress on brain circuitry associated with maternal behaviour. Overall, our study indicates that LN in mice may be a useful model to study neuroimmune relationships in certain aspects of PPD

An aptameric approach to interfering with Influenza's cap-snatching viral polymerase

Justine Beghin, Kira Sviderskaia, Kuldeep Kaur, Matthias Götte, Lorne Tyrrell, and Vanessa Meier-Stephenson

Supervisor: Vanessa Meier-Stephenson

INTRODUCTION

INTRODUCTION: Influenza viruses are a leading cause of pandemics, with an annual estimate of over 1 billion infections accounting for 500,00 deaths. Influenza virus is a multi-segmented, negative-stranded RNA virus, with many diverse strains due to its ability to reassort its genome segments. Transcription and replication of each segment is conducted by a trimeric RNA-dependent RNA polymerase (FluPol) through the process of cap-snatching, where the 5’ caps of host mRNAs are used for the viral RNAs. Since these processes are highly conserved it makes them good therapeutic targets. Aptamers are short oligonucleotides that fold to specifically fit certain binding spots, therefore making them a more druggable potential mechanism for targeting the FluPol complex. Can an aptamer-based approach be used to develop a small molecule therapeutic that targets FluPol?

METHODS

METHODS: The FluPol (Influenza A and B) complex will be produced using the Spodoptera frugiperda 9 (Sf9) insect cell line in a MultiBac system and purified using affinity column chromatography. Functional assays for in vitro replication and transcription will be optimized to test protein functionality after purification and how aptamer hit binding impacts the function of FluPol. After purification, the complex will be subjected to systematic evolution of ligands by exponential enrichment (SELEX) experiments to determine aptamer hits that can bind FluPol. Aptamers impacting either function of the FluPol will undergo structural analysis with cryoEM for better characterization of the binding site and modality.

RESULTS

RESULTS: Production of FluPol has been successful and is being optimized. FluPol complexes from influenza A and B viruses have been produced, purified, and are in the process of optimization. Functionality testing is underway, to be followed by SELEX experiments and structural analysis investigation.

CONCLUSIONS

CONCLUSIONS: Determining how aptamer binding affects FluPol functioning may lead to novel influenza therapeutic strategies.

Monitoring of Remote Ischemic Conditioning with an Adjunct Tissue Reflectance Sensor in Patients with Acute Ischemic Stroke and Small Vessel Disease: A randomized Control Trial

Gurpriya Bhangoo, Chetan KashinKunti, Robert Joseph Sarmiento, Nabeela Khan, Radhika Nair, Ahsan Majeed, Ashfaq Shuaib, Brian Buck, Michel Gauthier, Vivian Mushahwar, Martin Ferguson- Pell, Mahesh Kate

Supervisor: Mahesh Kate

INTRODUCTION

Remote ischemic conditioning (RIC) is a portable low-cost device-based intervention intended to induce ischemia tolerance and prevent target tissue injury. It is delivered by transient (5 min) pressure increase in the arm BP cuff by 30-50 mmHg above systolic BP to a maximum of 200 mmHg or increase in BP cuff pressure to a maximum of 200 mmHg irrespective of systolic BP. This inconsistency in transient pressure application may affect the fidelity of intervention delivery. We tested the hypothesis that monitoring RIC with an adjunct arm skin tissue reflectance sensor (STRS) device may be feasible in patients with acute ischemic stroke (AIS) and cerebral small vessel disease (cSVD).

METHODS

AIS patients with neurological deficits within 7 days of symptom onset were screened for moderate to severe cSVD. Eligible patients were randomized 2:1 to receive intervention RIC or sham RIC (7 days). The primary outcome measure was intervention and arm STRS feasibility. It was assessed as an intervention-related comfort by a 5-point Likert scale during each session (1-very uncomfortable, 5-very comfortable). The secondary outcome measure was the assessment of aSTRS-derived dermal blood concentration and blood oxygenation changes during RIC.

RESULTS

Fifty-one (34 intervention, 17 sham) patients were enrolled at a median (IQR) 39.7 (25-64) hours after symptom onset, with mean±SD age of 69±12.8 years, 24(47.1%) were females and median baseline NIHSS of 5(3-7). The Likert scale was similar 3.5 (3-4) in the intervention group and 4 (4-5) in the sham group. The aSTRS-derived blood concentration and blood oxygenation changes were proportionate to the arm pressure in the intervention arm compared to the sham arm (Figure).

CONCLUSIONS

RIC monitoring with aSTRS is feasible in patients with AIS and cSVD. Clinical trials assessing the efficacy of RIC intervention can consider aSTRS to assess the fidelity. Clinical Trial Registration Number: ClinicalTrials.gov ID: NCT05408130

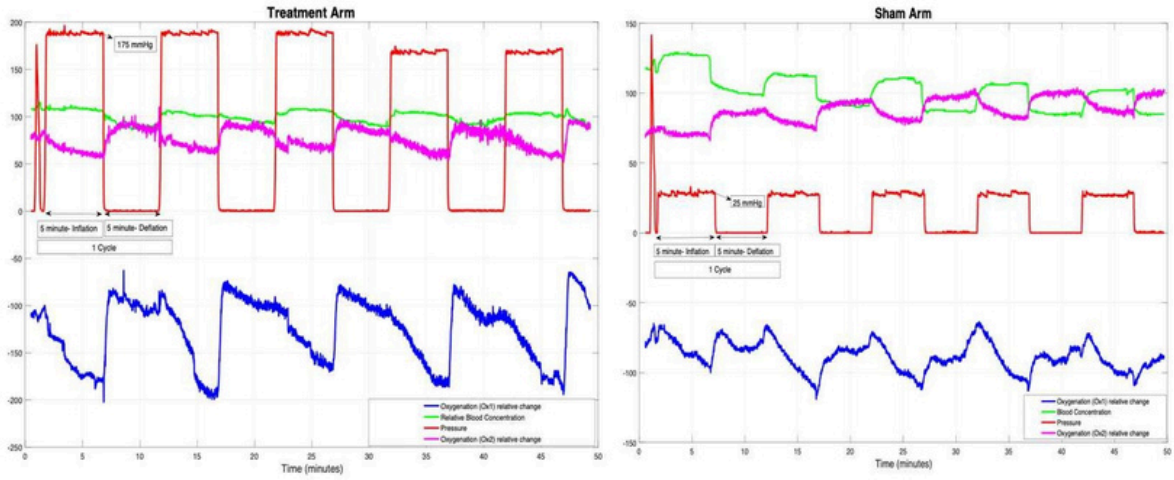


Figure: Remote Ischemic Conditioning Intervention and sham-treatment associated relative changes in arm skin tissue reflectance sensor. The treatment arm shows proportionate change in blood oxygenation (blue) to BP cuff pressure (red). In the sham arm the changes in blood oxygenation (blue) are variable and inconsistent to the BP cuff pressure (red).

Identifying guideline-concordant care after a severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in Alberta

Solmaz Bohlouli, Grace Lam, Sylvia Hao, Rachel Nguyen, Jason Randall, Michael Stickland, Scott W Klarenbach

Supervisor: Scott Klarenbach

INTRODUCTION

Understanding treatment patterns and medication adherence among individuals with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) allows the identification of treatment gaps and may inform opportunities to improve management and potentially alleviate the healthcare burden. The primary objective is to determine if COPD-related medication use post-emergency department visits or hospitalization for AECOPD meets the guideline-recommended step-up therapy. Secondary analyses are to identify factors associated with guideline-concordant care and measure adherence to medication post-discharge.

METHODS

A retrospective observational study using administrative data from Alberta will be performed. Individuals aged ≥ 35 years hospitalized, or emergency room visit for a COPD exacerbation (ICD codes J41, J42, J43, or J44) between January 1, 2017 -September 30, 2019 (index date) and resided in Alberta were identified. A table compared baseline COPD medication categories 6 months pre-index date and 6 months post-discharge and a multivariate logistic regression was conducted to identify factors associated with guideline concordant care and medication adherence.

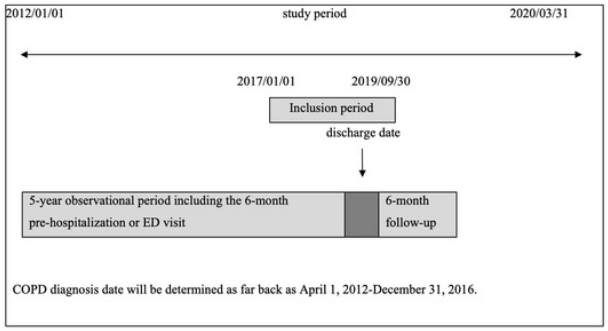
RESULTS

Work in Progress
Guideline concordance: addition/change in the category of baseline COPD medication categories post hospitalization.
Adherence: prescription-based medication possession ratio [MPRp] ≥0.80.
Independent variables: demographic variables clinical characteristics, specific comorbidities, index hospitalization, provider type and facility type post-discharge.

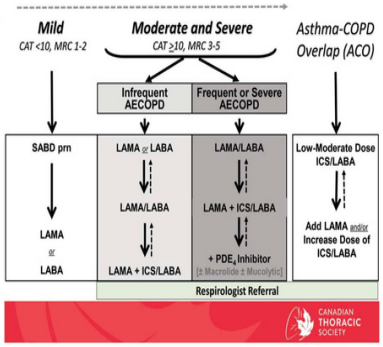
CONCLUSIONS

Guidelines are based on evidence-informed medication for optimal management of COPD exacerbation post-hospitalization; identifying the extent and scope of treatment gaps, and factors associated with treatment gaps, is important for clinicians and policymakers. This study will look at the proportion of COPD patients who received guideline-concordant care and the factors that contributed to receiving optimal care. Potential care gaps may exist if certain groups within the selected cohort did not receive concordant can post-discharge. Results may provide insight into the close consideration of guideline-based knowledge transfer strategies, and mechanisms to improve long-term medication adherence may improve outcomes.

Cohort selection



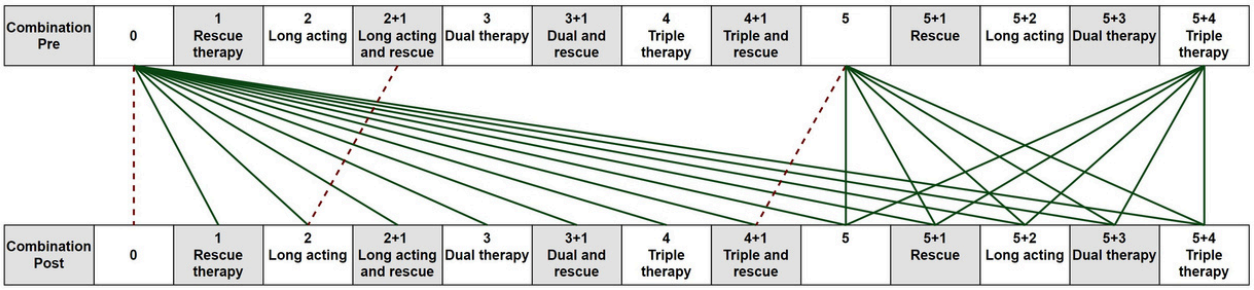
2017 CTS Guidelines



Baseline COPD medications

Code	Medication classes
0	None
1	SAMA or SABA or SAMA/SABA
2.1	LAMA
2.2	LABA
2.3	ICS
3.1	L AM A/ L ABA
3.2	I CS/ L ABA
4	ICS/LAMA/LABA (Triple)
5	PDE4 Inhibitor/Mucolytic/Azithromycin/Theophylline/Oral corticosteroids (Chronic use)

Sankey diagram for medication combinations pre and post



Correlating biophysical properties of TDP-43 aggregates with clinical phenotypes in amyotrophic lateral sclerosis and limbic-predominant age-dependent TDP43 encephalopathy

Maddison Charlton, Valerie Sim, Satish Nemani, Leonardo Cortez
Supervisor: Valerie Sim

INTRODUCTION

Aggregates of the protein TDP43 are found in several different neurodegenerative diseases, including frontotemporal dementia, amyotrophic lateral sclerosis (ALS) and limbic-predominant age-dependent TDP43 encephalopathy (LATE). We predict that distinct TDP43 aggregates are associated with these different diseases, a phenomenon known to occur in the hallmark protein folding disease, prion disease, where distinct protein conformations, or “strains”, cause distinct disease phenotypes.

METHODS

We propose to isolate TDP43 aggregates from ALS and LATE brain and determine which biophysical properties, if any, correlate with disease phenotype. TDP43 aggregates will be isolated from frontal cortex and hippocampus for LATE patients, frontal cortex, hippocampus, medulla, and spinal cord for ALS patients, and frontal cortex and hippocampus from cognitively normal individuals as controls. Isolates will be fractionated by size using asymmetric flow field-flow fractionation (AF4). Particle stability will be measured by conformational stability assay (CSA) and seeding efficiency by real time quaking conversion (RT-QuIC). The size, stability and seeding efficiencies of isolated TDP43 aggregates will be correlated with phenotype.

RESULTS

We are currently optimizing the isolation methods for TDP43 extraction. Using (list method here), we have found TDP43 protein in normal brain and frontal cortex of LATE brain. We expected that LATE brain TDP43 would be more prevalent in pellet fractions, given their aggregated state, but this was not the case. Instead, we modified the isolation protocol (list method) and applied it to frontal cortex and hippocampus from LATE brain, as hippocampus contains more TDP43 aggregates by pathology.

CONCLUSIONS

Once we optimize the isolation method, we complete our biophysical characterization and apply the method to our ALS samples. Our goal is to determine which biophysical properties are most correlated with phenotype.

Trends in the burden of ischemic heart disease among patients with chronic kidney disease in Alberta

Matthew Cooper, Feng Ye, Anukul Ghimire, Ikechi Okpechi, Gavin Oudit & Aminu Bello

Supervisor: Aminu Bello

INTRODUCTION

Ischemic heart disease (IHD) is a leading cause of mortality in patients with chronic kidney disease (CKD). The last decades have witnessed significant improvements in both IHD and CKD care. Information on the burden of IHD in the Canadian CKD population is limited.

METHODS

This is a population-based retrospective cohort study using a province-wide administrative database. The study cohort comprised adults ≥ 18 years old in Alberta with IHD and at least one outpatient serum creatinine measurement between May 1st, 2002 and March 31, 2019.

RESULTS

The age and sex standardized prevalence of IHD increased across all stages of kidney function. Compared to patients with an eGFR ≥ 60 ml/min, the rate of change in the prevalence of IHD was higher in patients with an eGFR 45-59 ml/min, with an annual rate of change of 0.86 (95% CI: 0.66 - 1.05; test for interaction p <0.001). Furthermore, compared to patients with an eGFR ≥ 60 ml/min, the annual incidence of STEMI significantly decreased in patients with eGFR 15-29 ml/min (incidence rate ratio [IRR]: 0.81; 95% CI: 0.76 - 0.87; p=0.004) and the annual incidence of NSTEMI significantly decreased in patients with eGFR 15-29 ml/min (IRR: 0.89; CI 95%: 0.86 - 0.92; p=0.019).

CONCLUSIONS

Between 2003 and 2019, the prevalence of IHD increased across all stages of CKD. Compared to patients with normal kidney function, the annual incidence of STEMI and NSTEMI decreased in patients with CKD stage 4. This information is important for the development of prevention strategies for IHD among patients with CKD.

Nanotubes mediated mitochondria transfer from normal to cancer cells promotes Mesenchymal-to-Epithelial Transition (MET) needed for the establishment of metastasis in cancer

Kléouforo-Paul DEMBELE, Alois Haromy, Jiyuan Piao, Gopi Sutendra, Evangelos D. Michelakis

Supervisor: Evangelos D. Michelakis

I**NTRODUCTION** Tumor metastasis is often incurable, killing most cancer patients. To metastasize, cancer cells receive signals from stroma cells to initiate Epithelial to Mesenchymal Transition (EMT) that allows them to metastasize. But to form metastatic colonies, EMT cells have to become epithelial again by undergoing MET, which is much less understood than EMT. We recently published how mitochondrial signals can remodel the cytoskeleton during EMT and how nuclear entrance of the mitochondrial enzyme Pyruvate Dehydrogenase can promote histone acetylation, required for EMT/MET. We hypothesized that MET is driven by the transfer of mitochondria from normal to cancer cells, through nanotubes, a feature of the r**emodeled cytoskeleton of EMT cells.**

METHODS (See below with results)

RESULTS Methods/results: CRISPR KO of Collapsin Response Mediator Protein 2A (CRMP2A, a microtubule associated protein) in lung cancer cells induces a full EMT phenotype associated with more metastasis in vivo. Using confocal imaging we found that these KO cells develop more/longer nanotubes with higher γ-tubulin levels, compared to parental cells and the same was true for other metastatic cells. To track specific mitochondria, we used lentiviral technology to generate cancer cells with stable GFP fluorescent mitochondria and normal liver epithelial cells with Mcherry fluorescent mitochondria. We set up 2D and 3D coculture models and found that EMT cells form more nanotube connections with epithelial cells through which they uptake intact mitochondria. Using cytometry to separate cells for analysis, we observed that cancer cells that uptake epithelial cell mitochondria, show an increase in epithelial/mesenchymal markers compared to cells that do not. Gatastatin, a specific inhibitor of γ-tubulin prevented nanotubes formation and mitochondria uptake and limited the EMT to MET transition.

CONCLUSIONS These preliminary findings suggest that γ-tubulin can be a previously unrecognized therapeutic target that can limit MET and thus metastasis, opening a much-needed new window in the MET/metastasis biology.

TSLP Secretion from Allergen-Treated Airway Epithelial Cells: Functional Role for Recycling Endosome Rab11a

Marc Duchesne, Luke Gerla, Paige Lacy

Supervisor:Paige Lacy

INTRODUCTION

Airway epithelial cells (AECs) are important environment-sensing cells that secrete alarmin cytokines, a subclass of asthma mediators that include thymic stromal lymphopoietin (TSLP). There is a fundamental lack of understanding of how AECs secrete TSLP. Previous research suggests that AECs may utilize recycling endosomes (REs) for secretion, regulated by Rab11a guanosine triphosphatase for trafficking to the cell membrane. We hypothesize that allergens induce TSLP release through the RE-specific trafficking regulator Rab11a.

METHODS

BEAS-2B and normal bronchial epithelial (NHBE) cells were used to examine AECs. AECs were seeded in BEGM cell culture media on glass coverslips in 6-well plates and stimulated for 8 h with cockroach extract (CE), house dust mite extract, or poly I:C. Stimulated AECs were examined by immunofluorescence (IF). A total of 10 cytokines were screened: IL-1β, -4, -6, -8, -13, -17, -25, -33, TNF-α and TSLP. AECs were also subjected to nucleofection with four different constructs of Rab11a siRNA, then stimulated with allergens. Coverslips were imaged and analyzed using Volocity imaging analysis software. Supernatant cytokine levels were quantified with MSD kits.

RESULTS

Allergens induced increased TSLP IF and secretion in AECs. CE-stimulated AECs showed significant increases in TSLP, TNF-α, and IL-33 IF at 8h stimulation ($p < 0.01$), while IL-4 and IL-1β decreased. Nucleofection with Rab11a shRNA demonstrated a reduction in intracellular TSLP IF and decreased TSLP secretion in response to CE. Findings were confirmed in primary cell cultures of NHBE cells.

CONCLUSIONS

Our results show, for the first time, intracellular localization of TSLP in AECs and co-labeling of TSLP with the RE regulator Rab11a. These findings suggest that TSLP may use REs regulated by Rab11a for its release following allergen stimulation. These discoveries are crucial for expanding our understanding of TSLP trafficking and the overall secretory apparatus in AECs in the context of allergen stimulation.

Uptake of SGLT2i and Outcomes in Patients with Diabetes and Heart Failure: A Population-Based Cohort and a Specialized Clinic Cohort

Luke R Gagnon Deepan Hazra, Kevin Perera, Kaiming Wang, Niharika Kashyap, Chandu Sadasivan, Erik Youngson, Luan Chu, Douglas C Dover, Padma Kaul, Scot Simpson, Aminu Bello, Finlay A McAlister, Gavin Y Oudit

Supervisor: Gavin Oudit

INTRODUCTION

Sodium/glucose cotransporter 2 inhibitors (SGLT2i) are efficacious in adults with diabetes mellitus (DM) and heart failure (HF) based on randomized clinical trials. We compared SGLT2i uptake and outcomes in two real-world cohorts: a population-based cohort of all adults with DM and HF in Alberta, Canada and a specialized heart failure clinic (HFC) cohort.

METHODS

The population-based cohort was derived from linked provincial healthcare datasets. The specialized clinic cohort was created by chart review of consecutive patients prospectively enrolled in the HFC between February 2018 and August 2022. We examined the association between SGLT2i use (modelled as a time-varying covariate) and all-cause mortality or deaths/cardiovascular hospitalizations.

RESULTS

Of the 4,885 individuals from the population-based cohort, 64.2% met the eligibility criteria of the trials proving the efficacy of SGLT2i. Utilization of SGLT2i increased from 1.2% in 2017 to 26.4% by January 2022 (Figure 1). In comparison, of the 530 patients followed in the HFC, SGLT2i use increased from 9.8% in 2019 to 49.1 % by March 2022 (Figure 1). SGLT2i use in the population-based cohort was associated with fewer all-cause mortality (aHR 0.51, 95% CI 0.41 – 0.63) and deaths/ cardiovascular hospitalizations (aHR 0.65, 0.54 – 0.77) (Figure 1). There were no significant differences in the community cohort for all-cause mortality (aHR 0.88, 0.52 – 1,20) and deaths/cardiovascular hospitalizations (0.81, 0.54 – 1.20) (Figure 1).

CONCLUSIONS

Despite robust randomized trial evidence of clinical benefit, the uptake of SGLT2i in patients with HF and DM remains low, even in the specialized HFC. Clinical care strategies are needed to enhance the use of SGLT2i and its full clinical benefit.

SGLT2i initiation in Heart failure patients with Diabetes

26%

Population Level SGLT2i users

46%

Specialized Heart Function Clinic SGLT2i users

SGLT2i usage at the start of 2022, over two years after the first RCT demonstrating benefit

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Adjusted Hazard Ratio for all-cause death for SGLT2i users

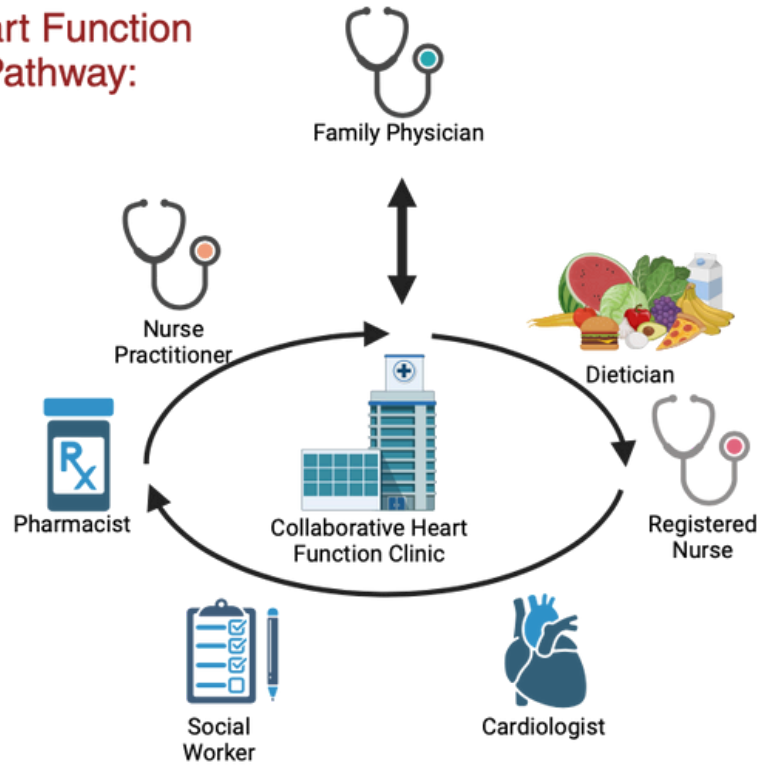
0.50 (0.53-0.74)

Population Level

0.81 (0.54-1.20)

Specialized Heart Function Clinic

Specialized Heart Function Clinic Care Pathway:



Outcomes Following Surgical Repair of Sinus Venosus Atrial Septal Defects: A retrospective study

Mathew N Hindi MD, Muhammad Moolla MD, Kevin John MD, Brody Jackson BSc, Anoop Mathew MD

Supervisor: Anoop Mathew

INTRODUCTION

Sinus Venosus Atrial Septal Defect (SVASD) is a rare type of non-primum and non-secundum defect that makes up 5-10% of all atrial septal defects. Left-to-right shunting leading to right-heart volume overload and arrhythmogenic disease are potential consequences of unrepaired defects. Surgical repair is the current standard of care, however newer transcatheter techniques are actively emerging. Studies to-date examining post-operative outcomes have been confined to small cohorts over short follow-up periods.

METHODS

We conducted a single-centre retrospective observational study analyzing long-term outcomes after surgical repair of SVASD. The primary outcome was mortality. Secondary outcomes encompassed atrial fibrillation, stroke, sinus node dysfunction, pacemaker insertion, pulmonary embolism (PE), right ventricle (RV) failure, reoperation, residual septal defect, vena cava obstruction, and reimplanted pulmonary vein obstruction.

RESULTS

Our study included 43 patients who underwent SVASD repair. The majority were female (62.8%) with 97.7% presenting with associated anomalous pulmonary venous connection. The median age was 50.9 years, and the mean follow-up period was 17.5 years. 20.9% were noted to have concomitant obstructive sleep apnea. Mortality rate was 4.7%. Incidences of atrial fibrillation, sinus node dysfunction, pacemaker insertion, PE, RV failure, and stroke over the long-term follow-up were 18.6%, 14.0%, 9.3%, 2.3%, 2.3%, and 2.3%, respectively. Reoperation, residual septal defect, vena cava obstruction, and reimplanted pulmonary vein obstruction were noted in 7.0%, 7.0%, 4.7%, and 2.3%, respectively.

CONCLUSIONS

Our data represents a comprehensive analysis of outcomes following surgical repair of SVASD at a large quaternary centre with one of the longest-term follow-up periods. The findings confirm the safety and efficacy of surgical repair of SVASD however the risk of post-operative arrhythmogenic disease is still significant. This establishes a reference point for evaluating emerging transcatheter therapies, which will require a non-inferior safety and efficacy profile for widespread adoption of these novel techniques.

The contribution of skin in neuromodulatory effects through transcutaneous spinal cord stimulation

Zahra Karamzadeh1,2 Jane Porter1,2, Vivian Mushahwar1,2,3,4

Supervisor: Vivian Mushahwar

INTRODUCTION

Injury to the spinal cord disrupt connection between the brain and the periphery, resulting in crucial motor and sensory deficits. Electrical neuromodulation techniques like transcutaneous spinal cord stimulation (tSCS) and epidural spinal cord stimulation (eSCS) offer promise for restoring sensorimotor function post-spinal cord injury by targeting distinct spinal networks. Computational modeling suggests comparable neuromodulatory impacts between tSCS and eSCS. However, previous research has not examined the involvement of cutaneous inputs in tSCS application.

METHODS

The current study aim is to investigate the influence of cutaneous sensory inputs on tSCS effect by attenuating cutaneous role using a topical anesthesia cream. To do this we enrolled twelve neurologically intact participants and employed a within-subject study design. Sensory perception threshold, maximal tolerance and two-point discrimination were examined to assess the effect of the anesthesia cream. applying two cream treatments over a 10×10 cm area of skin: 1) Versapro sham cream, and 2) Benzocaine 20%, Lidocaine 10%, and Tetracaine 4% (BLT) cream. A within-subject study design with two cream treatments applied to the skin over 10×10 cm: 1) Versapro sham cream, 2) Benzocaine 20%, Lidocaine 10% and Tetracaine 4% (BLT) cream. Additionally, we recorded the current amplitudes delivered by a DS8R (Digitimer, Welwyn Garden City, UK) stimulator required to produce equivalent spinal evoked potential (SEP) amplitudes in the biceps brachii muscle, assessing the neural excitability response to tSCS at cervical level of spinal cord.

RESULTS

The findings reveal a significant increase in sensory perception threshold, maximal tolerance, and two-point discrimination distance following BLT application. Moreover, maintaining SEP amplitudes constantly needed a significant rise in current amplitudes to achieve equivalent responses.

CONCLUSIONS

Results, suggesting the involvement of cutaneous inputs in modulating spinal excitability in response to tSCS.

Prevalence of metabolic-associated steatotic liver disease (MASLD) and its impact on adverse liver outcomes in patients with primary biliary cholangitis (PBC)

Kaviani, R. Wong YJ ; Shreekumar, D; Mason, AL; Montano-Loza, AJ; Lytvyak, E

Supervisor: Ellina Lytvyak

INTRODUCTION

MASLD is highly prevalent among Canadians, making coexistence with PBC inevitable. We aimed to determine the prevalence of MASLD in patients with PBC and the association between concomitant liver disease and adverse liver outcomes.

METHODS

Patients diagnosed with PBC between 1984 and 2023 and followed-up at the University of Alberta with vibration-controlled transient elastography data available were included.
MASLD was diagnosed if the Controlled Attenuation Parameter was equal to or greater than 288 dB/min in the presence of at least one cardiometabolic criterion. Proportions were compared using chi-square, medians – Mann-Whitney test. We utilized the Cox hazards regression model to determine the associations between MASLD and adverse liver outcomes.

RESULTS

A total of 115 patients (87.0% females, age at diagnosis 52.3±11.5 years) followed up over a median duration of 11.0 [range 0.1-39.7] years) were included. The prevalence of MASLD was 33.0% (n=38), with a tendency towards a higher prevalence among females (35.0%; n=35) than males (20.0%; n=3), although the difference was not significant (p=0.249). Frequencies of cirrhosis and decompensation over the course of the disease were similar between PBC patients with and without MASLD (50.0% vs. 50.6% (p=0.948); and 38.2% vs.37.1% (p=0.912), respectively). There was no association between MASLD and the development of cirrhosis (HR 0.51, 95%CI 0.23-1.13; p=0.095), decompensation (HR 0.81, 95%CI 0.37-1.76; p=0.596), liver transplantation (HR 0.72, 95%CI 0.19-2.72; p=0.628), or death (HR 0.69, 95%CI 0.22-2.16; p=0.519). PBC patients with MASLD have comparable event-free (median 10.7 [3.1-30.8] vs. 10.7 [0.1-23.3] years; p=0.684) and overall survival (median 11.3 [3.2-39.7 vs. 10.7 [0.1-23.3] years; p=0.456.

CONCLUSIONS

Every third patient with PBC had MASLD, which tended to be more prevalent among females. We did not observe any significant differences in the development of adverse liver outcomes between patients with PBC and concurrent MASLD in comparison to those without.

Impact of Sirolimus Proteinuria Following Liver Transplantation

Kaviani, R.; Kruger, M.; Ma, M.; Gonzalez-Abraldes, J.; and Bhanji, R.

Supervisor: Rahima Bhanji

INTRODUCTION

Sirolimus (Sr) is a potent immunosuppressant used in liver transplant recipients to prevent rejection in settings of calcineurin inhibitor toxicity. Sr can cause proteinuria though there are a lack of studies assessing its risk factors and their impact on clinical outcomes. We evaluated the incidence of proteinuria and its impact on clinical outcomes among liver transplant (LT) recipients who were Sr users compared with non-sirolimus (nonSr) users.

METHODS

We analyzed patients with their first LT between 2001 and 2020. Sr users received Sr for at least 6 consecutive months in the first year post-LT. We studied demographics, pre-LT comorbidities, and immunosuppression use. We evaluated the development of proteinuria, renal dysfunction, and cardiovascular disease. Data on post-LT infections, graft rejection, and patient survival were collected.

RESULTS

We analyzed 359 Sr and 762 non-Sr users (73.5% vs. 65% male). The average ages of Sr and non-Sr users were 54.9±9 and 51.7±11.6 years, respectively ($p<0.001$). Among non-Sr users, 95% were on tacrolimus and 67.8% were on mycophenolate. There were no differences in pre- LT chronic kidney disease (CKD), creatinine levels, or proteinuria. Sr users had a higher incidence of proteinuria (13.1% vs. 7.9%, $p=0.006$). Protein-creatinine ratios and albumin- creatinine ratios 12 months post-LT were not significantly different in Sr and non-Sr users ([40.1±105.6 vs. 57.5 ±169.9 mg/g, $p=0.39$], and [56.2±101.4 vs. 54.6±166.8 mg/g, $p=0.268$], respectively). Sr users had a significantly ($p<0.001$) higher incidence of post-LT CVD (24% vs. 14.8%), DM (20.4% vs. 12.6%), HTN (41.5% vs. 30.3%), and DLD (41.3% vs. 20.3%). There was no difference in post-LT CKD between Sr vs non-Sr (41% vs. 47%; $p =0.119$). Higher incidence of graft rejection was seen in Sr users (43.5% vs 27.8%, $p<0.001$).

CONCLUSIONS

Although Sr users were less likely to develop CKD post-LT, they had significantly higher rates of proteinuria, CVD, HTN, and DLD.

Double-Stranded DNA Breaks, FOXO1, and polysialylation define a novel therapeutic axis in diffuse systemic sclerosis (SSc)

Lamia Khan and Mohammed Osman
Supervisor: Mohammed Osman

INTRODUCTION

Systemic sclerosis (SSc), a life-threatening disease of unknown etiology. Its lethal complications stem from fibrosis driven by fibroblasts (FB). Patients with SSc develop variable disease courses with severe fibrosis in diffuse SSc (dSSc) patients and less severe in limited cutaneous SSc (lSSc). We recently showed that dSSc dermal FB have increased genomic instability with associated double-stranded DNA breaks (DSBs); and increased levels of the cancer-associated glycan polysialic acid (polySia). We also showed that dSSc patient treatment with autologous hematopoietic stem cell transplantation (dSSc-post-ASCT) resulted in decreased polySia, and polySia serum levels correlated with the severity of skin fibrosis. However, how genomic instability promotes polySia is currently unknown.
In cancer, DSBs activate the transcription factor forkhead box protein O (FOXO1) to promote cell survival. Therefore, I hypothesized that dysregulation of DSBs may promote aberrant polySia expression via FOXO1 activation in dSSc which normalizes post-ASCT.

METHODS

We recruited SSc patients (lSSc, dSSc, and dSSc-post-ASCT) who fulfilled the 2013 ACR/EULAR criteria. We generated primary FB using a 4 mm skin biopsy from each patient group, and from age/sex matched healthy controls (HC). We measured the frequency of DSBs, active (nuclear) FOXO1 and polySia levels via immunofluorescence/confocal microscopy and immunoblot. We also measured levels of the polySia synthetic enzymes (ST8Sia2/4) and pro-fibrotic signals via qRT-PCR (+/- pharmacological inhibition of FOXO1).

RESULTS

In dSSc FB, DSBs (*$p<0.05$), FOXO1(*$p<0.05$) and polySia expression (with associated ST8Sia2/4) were highest compared to lSSc and HC. Importantly, dSSc-post-ASCT FB had decreased levels of DSBs, FOXO1 activation (*$p<0.05$) and polySia. FOXO1 inhibition resulted in decreased fibrotic markers (e.g. fibronectin, CTGF), and ST8sia2/4 levels – suggesting that FOXO1 activation (potentially via DSBs) promote polySia and fibrosis.

CONCLUSIONS

Our study identifies a novel druggable DSB/FOXO1/polySia axis in dSSc patients. This axis may also serve as a novel biomarker for tracking disease progression and assessing treatment response.

Variation in risk-adjusted cardiac intensive care unit (CICU) length of stay and the association with in-hospital mortality: An analysis from the Critical Care Cardiology Trials Network (CCCTN) registry

Daniel M Koerber, Jason N Katz, Erin Bohula, Jeong-Gun Park, Mark W Dodson. Daniel A Gerber, Dustin Hillerson, Shuangbo Liu, Matthew J Pierce, Rajnish Prasad, Scott W Rose, Pablo A Sanchez, Jeffrey Shaw,... Sean Van Diepen

Supervisor: Sean Van Diepen

INTRODUCTION

Previous studies have suggested that there is wide variability in cardiac intensive care unit (CICU) length of stay (LOS); however, these studies are limited by the absence of detailed risk assessment at the time of admission. Thus, we evaluated inter-hospital differences in CICU LOS, and the association between LOS and in-hospital mortality.

METHODS

Using data from the Critical Care Cardiology Trials Network (CCCTN) registry, we included 22,862 admissions between 2017 and 2022 from 35 primarily tertiary and quaternary CICUs that captured consecutive admissions in annual 2-month snapshots. The primary analysis compared inter-hospital differences in CICU LOS, as well as the association between CICU LOS and all-cause in-hospital mortality using a Fine and Gray competing risk model.

RESULTS

The overall median CICU LOS was 2.2 (1.1-4.8) days, and the median hospital LOS was 5.9 (2.8-12.3) days. Admissions in the longest tertile of LOS tended to be younger with higher rates of pre-existing comorbidities, and had higher Sequential Organ Failure Assessment (SOFA) scores, as well as higher rates of mechanical ventilation, intravenous vasopressor use, mechanical circulatory support, and renal replacement therapy. Unadjusted all-cause in-hospital mortality was 9.3%, 6.7%, and 13.4% in the lowest, intermediate, and highest CICU LOS tertiles. In a competing risk analysis, individual patient CICU LOS was correlated ($r2 = 0.31$) with a higher risk of 30-day in-hospital mortality. The relationship remained significant in admissions with heart failure, ST-elevation myocardial infarction and non-ST segment elevation myocardial infarction.

CONCLUSIONS

In a large registry of academic CICUs, we observed significant variation in CICU LOS and report that LOS is independently associated with all-cause in-hospital mortality. These findings could potentially be used to improve CICU resource utilization planning and refine risk prognostication in critically ill cardiovascular patients.

Xanthogranulomatous Cholangitis: Rare, Benign Condition Mimicking Metastatic Cholangiocarcinoma

Kirollos Labib, Kirles Bishay

Supervisor: Kirles Bishay

INTRODUCTION

Xanthogranulomatous cholangitis is a rare entity only described in case reports. Thought to be an extension of xanthogranulomatous cholecystitis, it is presumed to be secondary bile extravasation into the gallbladder wall resulting in inflammation secondary to phagocytosis of bile pigment by macrophages, resulting in xanthoma cells. Pathology demonstrates histiocytes, lipid-laden macrophages, eosinophils, lymphocytes, plasma cells, and fibrosis indicating xathogranulomas. We present a case of xanthogranulomatous cholangitis without cholecystitis.

METHODS

Retrospective Chart Review of one patient and literature review of previous cases

RESULTS

Xanthogranulomatous cholangitis is an elusive diagnosis that mimics neoplastic disease. Pathology is difficult to attain and historical case reports required surgical resections and recently an EUS-guided FNA of the CBD. In our case, we attained the diagnosis through targeted liver biopsies. Pathology of xanthogranulomatous cholangitis typically demonstrates foamy histiocytes, lipid-laden macrophages, eosinophils, lymphocytes, plasma cells, and fibrosis indicating xathogranulomas. The pathogenesis is thought to be an extension of xanthogranulomatous cholangitis in which bile is extravasated into the gallbladder wall through Rokitansky-Aschoff sinuses or ulceration of the mucosa resulting in an inflammation caused by fibroblasts and macrophages as they phagocytose the lipids in bile, resulting in the formation of xanthoma cells. Ultimately, this case stresses the importance of pathological confirmation prior to surgical resection

CONCLUSIONS

Xanthogranulomatous cholangitis is a rare entity that often presents with jaundice, right upper quadrant pain and cholangitis symptoms. It is frequently associated with cholecystitis and can mimic carcinoma. A variety of sampling methods including surgical resection, core biopsy or endoscopic ultrasound-guided core needle biopsies demonstrating foamy histiocytes, lipid-laden macrophages, eosinophils, lymphocytes, plasma cells, and fibrosis indicating xathogranulomas is required to attain the diagnosis.

Nuclear Versus Cytoplasmic/Mitochondrial TRIM35 Signalling in Cardiomyocytes may Predict Irreversible Versus Reversible Cardiac Dysfunction and Chemotherapy-Induced Cardiotoxicity

Maria Areli Lorenzana-Carillo, Saymon Tejay, Farah Eaton, Michelle Mendiola Pla, Dawn E Bowles, John R Ussher, Evangelos Michelakis and Gopinath Sutendra

Supervisor: Gopinath Sutendra

INTRODUCTION

TRIM35 is predominantly a nuclear localized E3-ubiqutin ligase in cardiomyocytes, that functions to stabilize the levels of the pro-apoptotic transcription factor P53 and monoubiquitinate histone-2B, facilitating a more open chromatin state that exposes P53 transcriptional promoter sites. Notably, nuclear TRIM35 signaling is prominent in dilated cardiomyopathy (DCM). Here, we hypothesize its involvement in chemotherapy-induced cardiotoxicity (CIC), a potentially fatal condition associated with various standard cancer chemotherapeutics.

METHODS

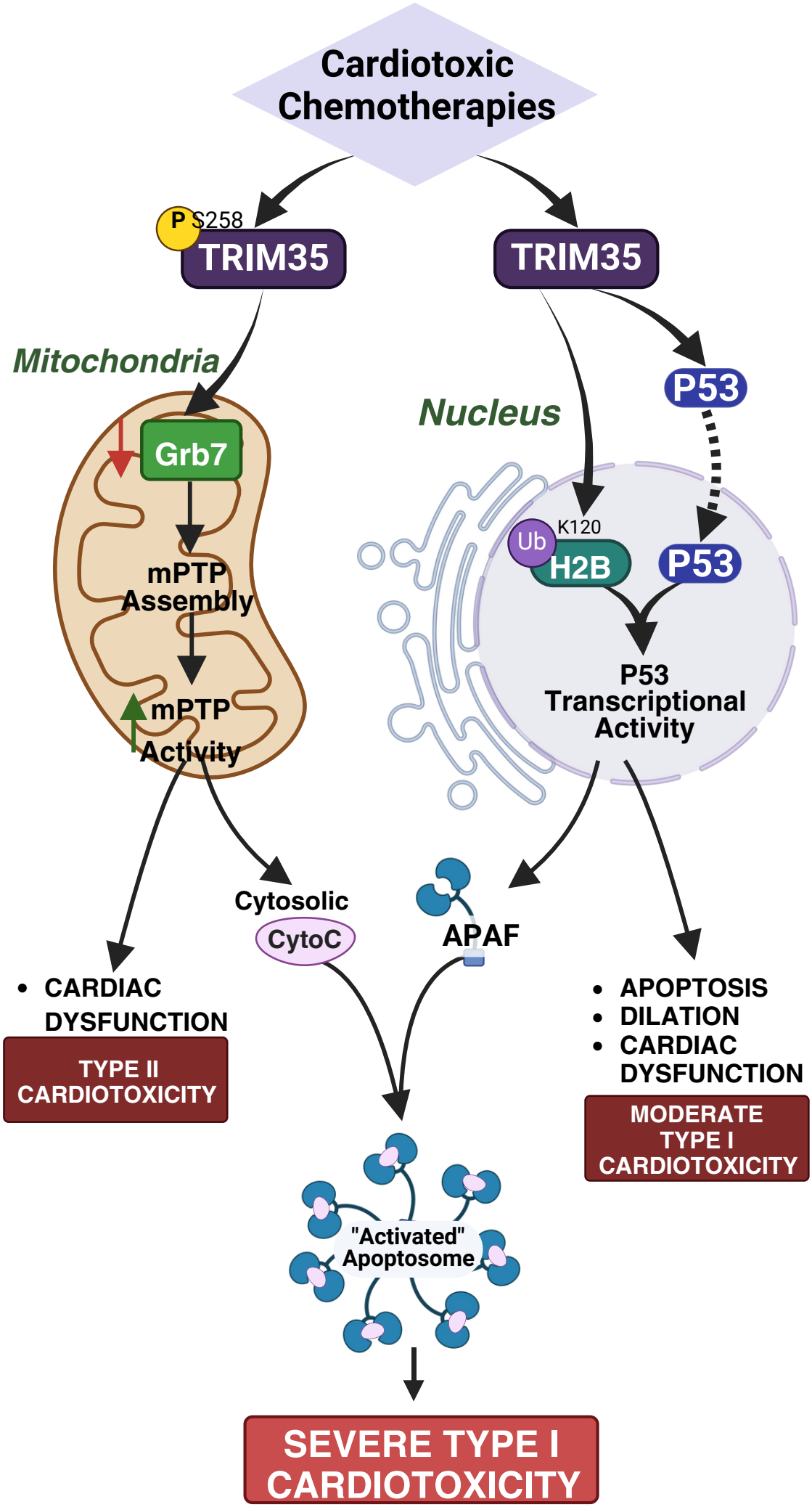
Immunofluorescence was employed to localize TRIM35. Chemotherapy agents were administered to assess their impact on cardiomyocyte apoptosis. We utilized cardiomyocyte-specific TRIM35 overexpressing mice and Grb7 deficient mice. Clinical relevance was explored through the analysis of human CIC left ventricle biopsies.

RESULTS

We found that standard chemotherapeutics can induce TRIM35 expression and, in several instances, trigger its phosphorylation at serine-258, situated within its nuclear localization sequence in cardiomyocytes, enhancing its cytoplasmic/mitochondrial localization. Moreover, we observed that cytoplasmic/mitochondrial TRIM35 ubiquitinates and degrades mitochondrial GRB7, crucial for ATP synthesis and preventing the assembly of the mitochondrial permeability transition pore (mPTP). Cardiomyocyte-specific deletion of GRB7 resulted in cardiac dysfunction characterized by decreased contractility without DCM development. Conversely, mice overexpressing TRIM35 in cardiomyocytes, where it predominantly localizes to the nucleus, displayed significant cardiac dysfunction and DCM. To evaluate whether nuclear versus cytoplasmic/mitochondrial TRIM35 influences reversible or irreversible cardiotoxicity, cardiomyocytes were treated with various known cardiotoxic chemotherapeutics. Those promoting S258P-TRIM35 exhibited decreased GRB7 expression but reduced cardiomyocyte apoptosis, while those inducing nuclear TRIM35 resulted in increased ub-H2B and P53 levels alongside significant cardiomyocyte apoptosis.

CONCLUSIONS

These findings unveil a new role for TRIM35 in CIC, suggesting cytoplasmic/mitochondrial TRIM35 may contribute to reversible CIC, whereas nuclear TRIM35 may drive irreversible CIC. Targeting TRIM35 pathways could offer novel therapeutic strategies for managing CIC and improving cancer patient outcomes, addressing a critical need in the field.


Cardiotoxic Chemotherapies
P S258
TRIM35
TRIM35
Mitochondria
Nucleus
P53
Grb7
mPTP Assembly
mPTP Activity
Ub
K120
H2B
P53
P53 Transcriptional Activity
Cytosolic
CytoC
APAF
• CARDIAC DYSFUNCTION
TYPE II CARDIOTOXICITY
• APOPTOSIS
• DILATION
• CARDIAC DYSFUNCTION
MODERATE TYPE I CARDIOTOXICITY
"Activated" Apoptosome
SEVERE TYPE I CARDIOTOXICITY

Peritoneal Dialysis-related Listeria monocytogenes Peritonitis Treated with Both Intravenous and Intraperitoneal Ampicillin – A Case Report and Literature Review

Scott MacKay, Benjamin W. Ewanchuk, & Mark McIsaac Supervisor: Mark McIsaac

INTRODUCTION

Listeria monocytogenes (L. monocytogenes) is a ubiquitous bacterium and opportunistic pathogen for immunocompromised patients. Peritoneal dialysis-related L. monocytogenes peritonitis is a rare clinical presentation, with a total of 23 cases reported to date and an overall mortality rate of 17.3%.

METHODS

The current report describes a case of peritoneal dialysis-related L. monocytogenes peritonitis in a 64-year-old female on long-term immunosuppressive therapies for a prior renal transplant. A summary of relevant literature is also included in this case report.

RESULTS

This patient was successfully treated with intraperitoneal ampicillin (125 mg/L in dialysate), in addition to intravenous ampicillin (1 gram every 12 hours) for 10 days and subsequent oral amoxicillin 500 mg every 12 hours to complete a total 21-day course of therapy. This treatment plan was based on pre-existing literature, though the dosing of intraperitoneal ampicillin was novel for the current report.

CONCLUSIONS

There is considerable variability in recommended antimicrobial dosing and frequency for peritoneal dialysis-related L. monocytogenes in existing literature, and our described antimicrobial therapy plan builds from these recommendations and was successful in treating this patient.

Table 3.

Summary of Documented Listeria monocytogenes PD-related Peritonitis Cases

Reference	Patient Sex, Age (Years)	Medical History	Presenting Symptoms	Antibiotics	Treatment Duration	Outcome
Ahmad et al. (2008)	Female, 28	SLE (on prednisolone and AZT), past PD peritonitis	Abdominal pain, conjunctivitis, cloudy effluent	IP cefazolin/ceftazidime à IP ampicillin	3 weeks	Resolved
Allais et al. (1989)	Female, 31	SLE	Abdominal pain, cloudy effluent	IP vancomycin à IP ampicillin	NR	Vancomycin failure à Resolved
Al-Wali et al. (1990)	Male, 53	GPA (on cyclophosphamide)	Abdominal pain, cloudy effluent	IP ampicillin + PO pivampicillin	3 weeks	Vancomycin failure à Resolved
Banerji et al. (1994)	Male, 64	Polymyositis (on prednisolone)	Abdominal pain, cloudy effluent	IP vancomycin/gentamicin à IP ampicillin/gentamicin	10 days à 4 weeks	Vancomycin failure à Resolved
Beckerleg et al. (1994)	Female, 59	T2DM	Fever, cloudy effluent, coma	IV vancomycin/ceftazidime à IV TMP-SMX	48 hours before death	Vancomycin failure à Died in hospital
Benjelloum et al. (2011)	Male, 64	Heart Failure, Tetralogy of Fallot	Abdominal pain, diarrhea, cloudy effluent	IP vancomycin/gentamicin	3 weeks	Vancomycin failure à Resolved
Bierhoff et al. (2011)	Male, 62	Heart Failure, Valvular Disease	Abdominal pain, fever, cloudy effluent	IP amoxicillin	3 weeks	Resolved
Bierhoff et al. (2011)	Male, 71	Tuberculosis	Fever	IV amoxicillin	6 weeks	Resolved
Boss et al. (2020)	Male, 72	T2DM, CAD	Abdominal pain, fever, cloudy effluent	IP cefazolin/ceftazidime à IV ampicillin + IP ampicillin	3 weeks	Resolved

Dryden et al. (1991)	Male, 60	CLL on prednisolone	Abdominal pain, fever, cloudy effluent	IV gentamicin + PO amoxicillin	10 days à 4 weeks	Vancomycin failure à Resolved
Hart et al. (1991)	Male, 67	Cirrhosis	Abdominal pain, cloudy effluent	IP vancomycin/gentamicin à IP ampicillin	NR	Vancomycin failure à Resolved
Korzets et al. (1989)	Female, 50	SLE on prednisolone and AZT	Abdominal pain, cloudy effluent	IP ampicillin/gentamicin	4 weeks	Resolved
Leduc et al. (2017)	Female, 81	NR	Cloudy effluent	IP amoxicillin + IV amoxicillin	4 weeks à 4 months	Resolved
Lunde et al. (1992)	Female, 38	SLE, past failed renal graft	Abdominal pain, diarrhea, cloudy effluent	IP ampicillin/tobramycin	2 weeks	Resolved
Mat et al. (2021)	Male, 64	IgA Nephropathy	Abdominal pain, fever, cloudy effluent, seizures	IV ampicillin/gentamicin + IP ampicillin	8 days before death	Died in hospital (heart failure)
Mitrovic et al. (2017)	Male, 57	Cirrhosis	Abdominal pain, fever, cloudy effluent	IP vancomycin/amikacin	48 hours before death	Vancomycin failure à Died in hospital
Moscovici et al. (2016)	Male, 70	Heart Failure, Valvular Disease	Septic shock, fever	IP ampicillin/gentamicin	3 weeks	Resolved
Myers et al. (1983)	Female, 71	ITP	Abdominal pain, cloudy effluent	IV erythromycin + IP erythromycin + IV TMP-SMX	NR	Resolved
Poulsen et al. (2018)	Female, 53	ADPKD (on prednisolone)	Abdominal pain, fever, cloudy effluent	IP vancomycin + PO ampicillin	2 weeks à 3 weeks	Resolved
Sia et al. (2017)	Female, 55	HIV, IgA Nephropathy	Abdominal pain, diarrhea, cloudy effluent, fatigue, anorexia	IP cefazolin/gentamicin à IP ampicillin	2 weeks	Resolved
Sin et al. (2021)	Male, 49	SLE (on prednisolone)	Abdominal pain, fever, cloudy effluent	IP cefazolin/gentamicin à IP vancomycin/ceftazidime/	3 days à 2 days à 4 weeks	Resolved

				amikacin à IP ampicillin/ amikacin		
Stylianou et al. (2008)	Male, 68	Prosthetic heart valves	Abdominal pain, conjunctivitis, fever, cloudy effluent	IP vancomycin à IP netilmicin	3 weeks à 6 weeks	Died in hospital (aspiration)
Tse et al. (2003)	Female, 38	SLE (on prednisolone and AZT)	Septic shock, fever, cloudy effluent	IV ampicillin/amikacin	4 weeks	Resolved

ADPKD = autosomal dominant polycystic kidney disease, AZT = azathioprine, CAD = coronary artery disease, CLL = chronic lymphocytic leukemia, GPA = granulomatosis with polyangiitis, ITP = immune thrombocytopenia, IP = intraperitoneal, IV = intravenous, NR = not reported, PO = per os, SLE = systemic lupus erythematosus, TMP-SMX = trimethoprim-sulfamethoxazole, T2DM = type II diabetes mellitus.

Comparing the Accuracy of Computed Tomography

Enterography to Balloon Assisted Enteroscopy in the Evaluation of Small Bowel Crohn's Disease

Jared Cooper, Scott MacKay, Matthew Reeson, Levinus A. Dieleman, Karen Kroeker, Shawn Wasilenko, Michal Gozdzik, Daniel C. Baumgart, Karen Wong, Farhad Peerani, Sergio Zepeda-Gomez, Edward Wiebe, & Brendan Halloran

Supervisor: Brendan Halloran

INTRODUCTION

Evaluation of small bowel Crohn's Disease (CD) relies on cross-sectional imaging such as computed tomography enterography (CTE) and small bowel endoscopy. Balloon-assisted enteroscopy (BAE) is the current diagnostic gold standard allowing for direct mucosal visualization. The accuracy of CTE in evaluating small bowel CD patients remains unclear compared to the gold standard of BAE.

METHODS

Patients with small bowel CD who underwent a CTE and BAE within a six-month period between 2011 and 2023 were reviewed. Relevant findings of active inflammation, long-segment disease, skip-segments, presence of strictures, and presence of high-grade strictures were extracted from both CTE and BAE studies and analyzed using BAE as the gold standard. Standard of care and expert interpretations by a radiologist with expertise in small bowel imaging were reviewed.

RESULTS

76 patients with 99 corresponding CTE and BAE pairings were identified. CTE was most sensitive for presence of active inflammation and strictures at 84.2% (74.4 -91.3) and 92.1% (83.6 - 97.1), respectively, and most specific for long-segment inflammation and high-grade stricture with specificities of 88.9% (78.4 - 95.4) and 91.2% (80.7 - 97.1), respectively. CTE showed poor sensitivity for high grade strictures (52.45% [36.4-68.0]) and long segment inflammation (58.3% [40.8-74.4]), and poor specificity for stricture detection (65.2% [42.7-83.6]). In patients with native bowel, CTE demonstrated improved detection of active inflammation with sensitivity of 86.1% [72.1 – 94.7] and specificity of 100% [29.2 -100]. In patients with post-surgical bowel, CTE demonstrated improved detection of high-grade strictures with specificity of 92.3% [74.9 – 99.1], though sensitivity remained low at 59.3% [38.8 – 77.6].

CONCLUSIONS

CTE performed best for detecting active inflammation and fibrostenotic disease. The detection of active inflammation was most accurate in native bowel and the detection of high-grade strictures was most accurate in post-surgical bowel. CTE and BAE remain complementary in informing management of small bowel CD.

Table 1. Computed Tomography Enterography (CTE) Compared to Balloon Assisted Enteroscopy (BAE) for the Assessment of Small Bowel Crohn's Disease for A) All included studies and B) Following Removal of Confounders Including Treatment Changes, BAE with Dilation Performed Before CTE, and Non-Traversable Stricture on BAE Post Dilation. CI: Confidence interval; PPV: positive predictive value; NPV: negative predictive value.

A)	Active Inflammation	Long Segment Inflammation	Skip-Lesions	Presence of Strictures	High-Grade Strictures
Sensitivity	84.2 (74.4 – 91.3)	58.3 (40.8 – 74.5)	82.6 (68.6 – 92.2)	92.1 (83.6 – 97.1)	52.4 (36.4 – 68.0)
Specificity	76.5 (50.1 – 93.2)	88.9 (78.4 – 95.4)	75.5 (61.7 – 86.2)	65.2 (42.7 – 83.6)	91.2 (80.7 – 97.1)
PPV	94.5 (87.9 – 97.6)	75.0 (58.6 – 86.4)	74.5 (64.2 – 82.7)	89.7 (83.3 – 93.9)	81.5 (64.5 – 91.4)
NPV	50.0 (36.3 – 63.7)	78.9 (71.5 – 84.7)	83.3 (72.3 – 90.5)	71.4 (52.3 – 85.1)	72.2 (65.2 – 78.3)

B)	Active Inflammation	Long Segment Inflammation	Skip-Lesions	Presence of Strictures	High-Grade Strictures
Sensitivity	80.0 (66.3 – 90.0)	50.0 (28.2 – 71.8)	86.7 (69.3 – 96.2)	93.0 (80.9 – 98.5)	60.9 (38.5 – 80.3)
Specificity	83.3 (51.6 – 97.9)	95.0 (83.1 – 99.4)	81.3 (63.6 – 92.8)	68.4 (43.5 – 87.4)	87.2 (72.6 – 95.7)
PPV	95.2 (84.9 – 98.6)	84.6 (57.2 – 95.8)	81.3 (67.5 – 90.0)	87.0 (77.4 – 92.9)	73.7 (53.7 – 87.1)
NPV	50.0 (35.2 – 64.8)	77.6 (69.3 – 84.1)	86.7 (72.0 – 94.3)	81.3 (58.3 – 93.1)	79.1 (69.1 – 86.5)

The lung-brain axis: Insights from a Mouse Model of Chronic Allergic Airway Inflammation

Shivani Mandal and Paul Forsythe

Supervisor: Paul Forsythe

INTRODUCTION

Asthma patients commonly experience a range of neurological comorbidities, such as anxiety, depression and sleep disorders. However, mechanisms driving the relationship between asthma and mood or behavior remain unclear. Here we utilized a mouse model to investigate the lung-brain axis in the context of allergic airway inflammation with the aim of gaining a better understanding of the biological basis for the association between asthma and mood disorders.

METHODS

6-week-old C57BL/6 female and male mice were sensitized and challenged with house-dust-mite (HDM) extract for 8 weeks to induce allergic airway inflammation. Histological changes in lung tissue and cell counts in bronchoalveolar lavage fluid (BAL) were assessed. Brain mast cell number and astrocyte activation in various brain regions were quantified by immunohistochemistry. Gene expression was assessed by short-read bulk mRNA sequencing.

RESULTS

HDM exposed mice demonstrated inflammatory cell infiltration in the lung and increased eosinophil count in BAL (p value<0.0002) confirming airway inflammation. In the brain, astrocytes activation was increased (p value<0.05) in the orbital area, hippocampus, and basolateral amygdala of mice with airway inflammation and this was more marked in females compared to males. Elevation in mast cell numbers was observed at the hippocampus-thalamus border (p value<0.01) in mice with airway inflammation. RNA sequencing results indicated changes in expression of genes linked to mood disorders and sleep regulation.

CONCLUSIONS

Our results indicate increased markers of neuroinflammation and changes in gene expression in the brain in response to chronic allergic airway inflammation. There is also preliminary evidence that there are sex-based differences in the brain response to airway inflammation. Future studies will use this model to better understand the mechanisms driving these observed changes. With this knowledge we hope to inform strategies for better management of mood and behavioral comorbidities in asthma.

Examining the impacts of combining functional electrical stimulation assisted arm and leg cycling with epidural spinal cord stimulation after a motor complete spinal cord injury: A case study

Darren J. Mann, Monique Yuan, Adalberto Loyola-Sanchez, Srijana Gautam, Saba Allahgholiloo, Jane A. Porter, Zahra Karamzadeh, Vivian K. Mushahwar

Supervisor: Vivian Mushahwar

INTRODUCTION

Previous studies in our lab have demonstrated that functional electrical stimulation assisted arm and leg cycling has been an effective rehabilitative intervention following a spinal cord injury (SCI). However, the effects of combining epidural spinal cord stimulation (eSCS) with this rehabilitative exercise paradigm remain unknown. Subsequently, we hypothesize that pairing eSCS with functional electrical assisted arm and leg cycling will improve motor/sensory function, decrease spasticity, and increase the amount of resistance that the participant is able to do during training.

METHODS

This novel case study paired eSCS with functional electrical stimulation assisted arm and leg cycling in an individual with a motor complete SCI. The individual participated in this program for 1 hour every day 5 days a week for a total of 12 weeks. Assessments that were administered focused on changes in motor/sensory function, spasticity and changes in resistance while biking. To assess these respective outcomes the International Standards for Neurological Classification of Spinal Cord Injury, the Modified Ashworth Scale and the total work done were measured.

RESULTS

Findings from the 12 weeks of training indicate that the impact of eSCS on motor/sensory function is inconclusive, that spasticity generally decreased and that there was a general trend of an increase in resistance level that was able to be accomplished during training. Future studies will attempt to delineate both the ascending and descending impact that eSCS has on spinal circuitry.

CONCLUSIONS

Ultimately, this study provides evidence, for the first time, about the impact that eSCS neuromodulation combined with functional electrical stimulation assisted arm and leg cycling has after a motor complete SCI. Moreover, this study provides information about the long-term plasticity that occurs through interlimb coupling. The changes observed in spasticity and resistance could be used to help improve quality of life and functional mobility after SCI.

Cultured human Pulmonary neuroendocrine cells stimulated with House dust mite allergen activate Innate lymphoid cells 2 and classic Dendritic cells 1

Ritu Mann-Nuttel, Nami Shrestha, Yingqi Wu, Harissios Vliagoftis and Paul Forsythe

Supervisor: Paul Forsythe

INTRODUCTION

Pulmonary neuroendocrine cells (PNEC) have recently gained attention as rare airway epithelial cells that amplify allergic asthma responses. PNEC derived mediators such as Calcitonin gene-related peptide (CGRP) have been shown to activate Innate lymphoid cells 2 (ILC2) in a murine asthma model. Studying human PNEC function has been challenging due to a lack of suitable cell isolation methods. Here used our novel in vitro human PNEC model and investigated the effect of supernatant from PNEC stimulated with House dust mite allergen (HDM) on ILC2 and classic dendritic cell (cDC) activation.

METHODS

PNEC enriched cultures were generated from primary bronchial/tracheal epithelial cells (ePNEC) in transwells. Successful differentiation of neuroendocrine cells was evaluated with qRT-PCR and immunohistochemistry. In all experiments, standard (PNEC deficient) human bronchial/tracheal epithelial cells served as controls. At day 60 of culture, ePNEC were challenged with HDM for 24h and supernatant was subsequently used to stimulate PBMC-derived Lin- CD45+ CRTH2+ IL13+ IL5+ ILC2 and Lin- CD11cint CD141+ cDC1, Lin- CD11cint CD1c+ cDC2 and Lin- CD14+ HLA-DR+ CD141- DC3 cells. ILC2 and DC cell activation was assessed with flow cytometry.

RESULTS

Supernatant from HDM stimulated ePNEC induced an 60% increase in ILC2 cells expressing IL13 and IL5 compared to control. Further, the activation markers MHCII and CD86 were significantly upregulated in cDC1 cells exposed to mediators from HDM stimulated PNEC, but not in cDC2 or DC3 cells.

CONCLUSIONS

Here we demonstrate, for the first time, that HDM stimulates human PNEC to release mediators that activate ILC2 and cDC1 cells. These results highlight or novel model as an effective tool for investigating neuro-endocrine immune interactions in the human airway and that will contribute to a deeper understanding of PNEC biology in asthma development and severity.

A description of orientation and technological support strategies provided in Internet or mobile-based health interventions (IMIs) for adult patients.

Julian Mansour, anonymous (researcher), Kathleen Ismond, Holly Minckler, Elizabeth Dennett, Ben Vandermeer, Puneeta Tandon

Supervisor: Puneeta Tandon

INTRODUCTION

With the ubiquity of modern technology, an underlying assumption is that new IMI users can quickly learn how to navigate and utilize the novel IMI. Orientations and technology supports help facilitate IMI participant interactions, yet despite their perceived utility, infrequent studies have reported on this topic. We hypothesized that orientations and technology support would improve patient accessibility and usage with IMIs. Our objectives are to identify the presence and modalities of orientation and technology supports in IMIs, and describe associations between them with adherence and completion rates.

METHODS

The PRISMA extension for scoping reviews guided the activities. A search of EMBASE, MEDLINE, and Scopus databases was completed on Nov 30, 2023. English language articles studying adults (≥18 years) patients enrolled in an IMI were included. Studies were excluded if the IMI was SMS-only, survey-only, or lacking multimedia content. Screening and full text review were done, and abstracted data includes the IMI, participant descriptions, orientation and technology supports, and measurements of IMI adherence and completion.

RESULTS

1,960 unique studies were retrieved, and 88 made it to final abstraction. The overall mean age was 48.5 years, and the top three patient conditions were: pre/post-op (15.9%), neurological (14.8%), and musculoskeletal (11.4%). Only 43 (48.9%) IMIs had an orientation, with top three modalities being in-person (30.7%), training manuals (4.5%), or in-app tutorials (3.4%). 38 (43.2%) studies offered technology support, with top three modalities being phone calls (14.8%), in-app chats (6.8%), and emails (5.7%).

CONCLUSIONS

Our work identifies a gap in providing onboarding and technology assistance to adults in IMIs. To ensure accessible and equitable care for all, future IMIs may wish to improve delivery of orientation and technology support. Associations between age and orientation/technology support with adherence and completion are under evaluation.

Thymic stromal lymphopoietin (TSLP) expression in nasal epithelial cells: Elevation in severe asthma

Hazel Marriott, Marc Duschesne, Isobel S Okoye, Luke Gerla, Irvin Mayers, Jalal Moolji, Adil Adatia, Subhabrata Moitra and Paige Lacy

Supervisor: Paige Lacy

INTRODUCTION

The secretion of alarmin cytokines by epithelial cells, including thymic stromal lymphopoietin (TSLP), interleukin (IL)-25, and IL-33, heralds the onset of the asthma inflammatory cascade and immune effector infiltration. This has led to the development of monoclonal antibodies to target alarmin cytokines, including tezepelumab, a human monoclonal against TSLP. However, alarmin cytokine expression in the upper airways in asthma remains largely unknown. We hypothesize that nasal epithelial cell expression of TSLP correlates with asthma severity.

METHODS

Epithelial cells derived from buccal, nasal and throat brushings were collected from patients with varying asthma severities that were stratified according to GINA-1/2, -3, -4 and -5 classifications and compared with healthy controls (n=10 per group). Intracellular alarmin cytokine expression in cells from brushings was assessed using flow cytometry using fluorescence minus one (FMO) controls. Separate single cell suspensions were generated from the collections to determine viability. Following viability assessment, cells were incubated with a mixture of primary antibodies to detect alarmin cytokines, the leukocyte marker CD45 and the epithelial cell marker cytokeratin 8 (Ck8). Cells were analyzed using a Fortessa-SORP cytometer.

RESULTS

Ck8+ nasal epithelial cells derived from GINA-5 patients had significantly elevated expression of TSLP as compared to GINA-1/2, -3, and -4 asthmatics ($p<0.05$), after adjusting for age and sex. Additionally, TSLP levels were not altered in association with nasal comorbidities, indicating that these comorbidities do not affect TSLP expression. No significant changes in IL-25 or IL-33 were observed.

CONCLUSIONS

Our study demonstrates for the first time that nasal Ck8+ epithelial cells from GINA-5 asthmatics express elevated levels of TSLP. These findings suggest that nasal brushings may provide effective surrogate biomarkers for understanding the alarmin dysregulation in severe asthma. Further work is ongoing to correlate TSLP expression in nasal epithelia with asthma severity and response to biologic therapy including tezepelumab.

SGLT-2 Inhibitor Use in Adults (Age ≥ 65) with Diabetes and Cardiovascular Disease is Lower in Alberta and Manitoba than in Ontario: A Cross-Sectional Study

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Supervisor: Darren Lau

INTRODUCTION

Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have end-organ benefits for patients with type 2 diabetes and cardiovascular disease (CVD). Despite identical indications for SGLT2i, public drug formulary and co-pay/deductible coverage policies differ by province. We aimed to estimate the association of prior authorization, compared to regular benefit status, on SGLT2i use in adults with diabetes and CVD.

METHODS

Cross-sectional study of Canadians age ≥ 65 years with diabetes and CVD prescribed ≥1 antihyperglycemic agent from 2018 to 2020, using electronic medical record data from primary care practices across Canada. We compared SGLT2i use in Alberta and Manitoba, where SGLT2i required prior authorization, to Ontario, where SGLT2i were regular benefits. Notably, Manitoba differs from Alberta and Ontario in imposing income-based deductibles on all eligible residents. We also examined metformin and sulfonylureas, and dipeptidyl peptidase-4 inhibitors (DPP4i), as negative and positive controls, respectively. We used Poisson regression to estimate confounder-adjusted prevalence ratios for the use of each medication.

RESULTS

Our sample included 3,191 adults (average age 75 years, 31% female). SGLT2i use was lowest in Manitoba (15.6%), then Alberta (25.9%), and highest in Ontario (31.9%). Compared to Ontario, prescriptions for SGLT2i remained lower in Alberta after adjustment (prevalence ratio [PR] 0.79, 95% CI [0.70-0.90], $p < 0.001$) and Manitoba (PR 0.46 [0.37-0.57], $p < 0.001$) (table 1). Metformin use was similar between provinces. DPP4i use was much lower in Alberta and Manitoba than in Ontario. Manitoba had a much higher sulfonylurea prevalence in this sample than Ontario.

CONCLUSIONS

SGLT2i use was lower in Alberta and Manitoba, where these medications were subject to prior authorization and/or income-based deductibles, compared to Ontario. Our results highlight the need for ongoing and timely re-evaluation of formulary restrictions to avoid inadvertently foregoing the proven cardiovascular and kidney benefits of SGLT2i and similar novel cardiometabolic therapies.

Table 1: Poisson regression analysis for SGLT2i use in adults with CVD (n = 3,191)

	Prevalence Ratio (95% Confidence Interval)		
	Model 1	Model 2 Comorbidities	Model 3 Comorbidities + Medications
Province			
Ontario	1.00 (ref)	1.00 (ref)	1.00 (ref)
Alberta	0.81 (0.71, 0.92)	0.74 (0.65, 0.84)	0.79 (0.70, 0.90)
Manitoba	0.49 (0.40, 0.60)	0.42 (0.34, 0.51)	0.46 (0.37, 0.57)
Comorbidities			
Age (years)			
65-74		1.00 (ref)	1.00 (ref)
75-84		0.74 (0.66, 0.84)	0.74 (0.66, 0.84)
≥ 85		0.32 (0.23, 0.45)	0.33 (0.24, 0.46)
Female		0.76 (0.67, 0.86)	0.78 (0.68, 0.88)
HF		0.99 (0.84, 1.17)	1.01 (0.86, 1.20)
CKD			
Stage 0 (eGFR >90, ACR < 3)		1.00 (ref)	1.00 (ref)
Stage 1 (eGFR >90, ACR ≥ 3)		1.04 (0.76, 1.41)	1.04 (0.77, 1.41)
Stage 2 (eGFR 60-89)		0.92 (0.72, 1.17)	0.91 (0.72, 1.15)
Stage 3 (eGFR 30-59)		0.80 (0.62, 1.03)	0.79 (0.62, 1.02)
A1c			
≤ 7.0%		1.00 (ref)	1.00 (ref)
7.1 to ≤ 8.5%		1.87 (1.65, 2.11)	1.88 (1.66, 2.13)
> 8.5%		1.91 (1.63, 2.25)	1.94 (1.64, 2.29)
Current Medications			
Insulin			0.99 (0.87, 1.13)
Statin			1.35 (1.15, 1.58)
ACEi/ARB			1.17 (1.02, 1.34)

A1c, glycated hemoglobin; *ACEi*, angiotensin-converting enzyme inhibitor; *ACR*, urine albumin-to-creatinine ratio; *ARB*, angiotensin receptor blocker; *CKD*, chronic kidney disease; *CVD*, cardiovascular disease; *eGFR*, estimated glomerular filtration rate (mL/min/1.73 m^2); *HF*, heart failure; *SGLT2i*, sodium-glucose cotransporter-2 inhibitor.

Variability in lung transplant clinical practices in Canada: Preliminary results of a national survey

Margret Michaels, Karina Kaur, Jason Weatherald, Jayan Nagendran Meghan Aversa M, Roland Nador , Charles Poirier , Kieran Halloran

Supervisor: Jason Weatherald

INTRODUCTION

There is heterogeneity in outcomes after lung transplant, and the degree to which variation in clinical practice contributes to this is unknown. We sought to quantify the averages and variance in practices among Canadian lung transplant centres via a physician and surgeon national survey.

METHODS

We conducted a cross-sectional digital survey via email of all physicians and surgeons in all Canadian lung transplant centres, including surgical and satellite centres. (perform transplants and provide care pre- and post-) and non-surgical surgical centres (provide care pre- and post-). We analyzed the data via chi square tests, t-tests, and Wilcoxon rank sum tests.

RESULTS

We identified 55 clinicians across Canada, and 46 (84%) completed the survey. We restricted this analysis to the 38 respondents from surgical centers (22 physicians, 16 surgeons) who were most frequently: male (68%); had practiced for 10+ years (61%); performed all or a majority of their work in lung transplant (61%); and practiced in an academic setting (100%).
Table 1 depicts a selection of responses.
Significant variation was noted in: the presence of an upper age limit; the BMI upper limit; performing single lung transplants, deceased donor lobar transplants, heart-lung, combined lung-abdominal organ, and simultaneous CABG; and the presence of a donor age limit. The average rank order and variation in allocation priorities are depicted in Figure 1.

CONCLUSIONS

We noted substantial variation in some basic aspects of lung transplant clinical practice. We will expand our analysis with all comprehensive survey elements, non-surgical centre data, and within-center variation.

PRIORITIES FOR FUTURE LUNG TRANSPLANT RESEARCH: A PRELIMINARY REPORT FROM A JAMES LIND ALLIANCE PRIORITY SETTING PARTNERSHIP

Margret Michaels, Kieran Halloran , Lea Harper, Tamara Rader, Nikki Marks Céline Bergeron, Rowan Sargeant, Eileen Leopold, Basil S. Nasir, Jason Weatherald

Supervisor: Jason Weatherald

INTRODUCTION

Lung transplantation is vital for end-stage lung disease treatment, yet enhancing outcomes requires further research. The Lung Transplantation Priority Setting Partnership (PSP) aims to unite patients, caregivers, and clinicians in identifying and prioritizing uncertainties for future research. By aligning research and funding with stakeholders' goals, the PSP ensures focused efforts on critical areas needing
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2) Identifying research questions and uncertainties with an initial survey
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The output is a top-10 list of uncertainties for future research.

RESULTS

Here we report the preliminary results of the initial survey for Alberta, Canada only.
With 76 respondents, including 33% patients, 12% caregivers, and 55% clinicians (physicians: 16, nurses: 15, allied health: 11), the survey received 172 unique questions. These were categorized into topics, with 169 deemed relevant and 3 irrelevant. Of these questions, 31% came from patients, 6% from caregivers, and 61% from clinicians.
Topics proposed included:
-Prognosis (n = 30)
-Education (n = 26)
-Recipient evaluation and selection (n = 26)
-Immunosuppression (n = 19)
-Patient and caregiver support (n = 18)
-acute rejection (n = 10)
-Chronic lung allograft dysfunction (n = 10)
-Transplant team and care delivery (n = 9)
-complications (n = 7)
-Infections (n = 6)
-Donor selection and management (n = 4)
-Extra-corporeal life support (n = 3)
-Bioengineering artificial grafts (n = 1)

CONCLUSIONS

Stakeholders in lung transplant research in Alberta, Canada, identified unique

questions for
future research. The next steps include broadening the survey across Canada, verifying uncertainties against the existing literature, interim prioritization, and a final virtual workshop to establish the top 10 research uncertainties.

Immune checkpoint inhibitor liver-related adverse events: A Case Series

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Supervisor: Aldo Montano-Losa

INTRODUCTION

Immune-related adverse events (IRAE) are rising due to increasing use of immune checkpoint inhibitors (ICI) for cancer treatment. Liver-related adverse events occur in 5 to 10% of patients, with immune-mediated hepatitis (IMH) accounting for majority of cases. <3% result in severe hepatitis and <0.04% fulminant hepatitis. Severity is determined by the degree of LE (liver enzyme) elevation, which determines treatment. Most patients with mild to moderate hepatitis respond to discontinuation of ICI. In severe cases, immunosuppression is required with corticosteroids and/or a secondary immunomodulator. ICI-related biliary complications are less common and account for <3% of IRAE. Specifically, ICI-related sclerosing cholangitis (IRSC) is rare and accounts for <1% of cases. The pathogenesis of IRSC is not well understood and patients are typically refractory to corticosteroids. This case series reports seven patients who received ICI and developed liver-related adverse events.

METHODS

Patient were identified as having a LRAE and charts were manually reviewed.

RESULTS

Seven patients were identified to have IMH and/or IRSC during the study period. Five patients developed IMH requiring immunosuppression, one IRSC, and one IMH and IRSC. Five of six patients with IMH developed severe hepatitis and required corticosteroid therapy. Three of these patients required a secondary immunomodulator with mycophenolate mofetil or azathioprine. Five of six patients with IMH had normalization of LE. ICI therapy was only restarted in one patient. Two patients developed IRSC with cholestatic LE elevation and imaging suggesting sclerosing cholangitis. One patient was started on ursodeoxycholic acid, and the other patient had spontaneous normalization of their LE and radiographic improvement of biliary dilation.

CONCLUSIONS

Liver-related adverse events are becoming more common with widespread use of ICI. Patients should have baseline LE completed and frequent monitoring while on therapy. Prompt recognition of elevated LE is critical in the diagnosis of IMH. Further prospective data is required to establish diagnostic criteria and treatment guidelines.

Development of a culturally appropriate, community-delivered management program for urinary incontinence in Sikh women – reflections on community engagement

Simran Panesar, Saima Rajabali, Adrian Wagg

Supervisor: Adrian Wagg

INTRODUCTION

Urinary incontinence (UI), the involuntary loss of urine is a distressing symptom in women, and stigma attributed to cultural attitudes and beliefs can prevent South Asian women from seeking care for UI. There are no data on Sikh women regarding their views on UI. The objective of this study is to explore how older Sikh women (>65) view UI, through a cultural/feminist lens. This reflexive piece focuses on the research team's experience of engaging the Sikh community to form an advisory group for the project.

METHODS

The University of B.C. Community Engaged Learning Reflection Framework was used to build the foundation for engagement with the Sikh community in Edmonton. Connections/networks among Sikh community members were utilized in a snowballing technique, to reach the group of five women who agreed to form the research advisory group. Through monthly advisory meetings, community partners will provide advice on recruitment strategies, interview questions, setting, and phrasing of English terms like UI, into Punjabi, which will be vetted by Punjabi language teachers.

RESULTS

It has been challenging to reach our target population, given the participants' lack of trust, and cultural and religious barriers preventing open conversations on UI. We started by directly approaching older women in Sikh gurdwaras, but women showed reluctance to engage. This difficulty was addressed by engaging younger/ middle-aged Sikh women to garner trust/support from older members. As informed by collaborators, an important requirement for interviews is creating a 'safe space'.

CONCLUSIONS

Community engagement of older Sikh women can be challenging because of cultural and religious barriers associated with the taboo topic of UI. A multi-faceted approach was required to engage older Sikh women to form an advisory group to guide the next phase of our study (qualitative interviews). The results of this study will inform the design of a culturally appropriate, management program for UI.

Impact of co-morbid Heart Failure on health outcomes

following hospitalization for AECOPD

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Supervisor: Mohit Bhutani

INTRODUCTION

Heart Failure (HF) is common in patients with chronic obstructive pulmonary disease (COPD). The impact of concomitant HF on outcomes in patients hospitalized for an acute exacerbation of COPD (AECOPD) is uncertain.

METHODS

This was a population-based cohort study of all patients hospitalized for an AECOPD in Alberta, Canada between September 2018 to December 2019 using linked administrative databases with a diagnosis of COPD at discharge. The exposure of interest was a diagnosis of HF based on a validated ICD-10 algorithm, defined as 1 inpatient or 2 ambulatory heart failure visits within 1 year of each other anytime within the 5 years prior to the index admission for AECOPD (1). The primary outcome was 30-day all-cause hospital readmission. Secondary outcomes were 30-day all-cause emergency department (ED) visits and all-cause 90-day mortality post-discharge. We used Poisson regression and Cox proportional hazards regression to compare outcomes between patients with and without HF.

RESULTS

Of 8463 patients hospitalized with an AECOPD, the median age was 74 years, 49.8% were female, and 33.3% of patients had concomitant HF. The 30-day all-cause readmission, ED visit, and 90-day mortality rates were significantly higher in patients with HF (see Figure 1).

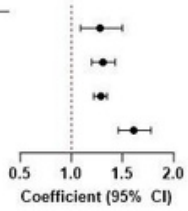
CONCLUSIONS

Comorbid HF is associated with increased short-term risk of all-cause readmission, ED visits, and death in patients following hospitalization for an AECOPD. Further research will identify whether medical optimization of both COPD and HF at the time of discharge impacts the short-term risk.

References

1. Schultz SE, et al. Chronic Dis Inj Can. 2013;33(3):160–6

Outcome	AECOPD, no HF (n=5,647)	AECOPD + HF (n=2,815)	Coefficient (95% CI)
Total hospital readmission in 30-days	1108	782	1.61 (1.46, 1.78)[a]
Total ED visits in 30-days	5026	3136	1.29 (1.22, 1.35)[a]
> 1 ED visit in 30 days (%)	1095 (19.4%)	729 (25.9%)	1.31 (1.20, 1.43)[b]
All-cause mortality in 90-days (%)	350 (6.2%)	339 (12.0%)	1.28 (1.09, 1.50)[c]



All models are adjusted for age, sex, rural residence, Charlson comorbidity index, median income, and social deprivation index. Coefficients are expressed as [a]realtive risks (RR), [b]prevalence ratio (PR), and [c]hazard ratio (HR) obtained from [a]Poisson regression, [b]modified Poisson regression, and [c]Cox proportional hazard models.

AECOPD: acute exacerbation of chronic obstructive pulmonary disease, CI: confidence interval, ED: emergency department, HF: heart failure

Figure 1A: Association between HF and outcomes among patients hospitalized for AECOPD.

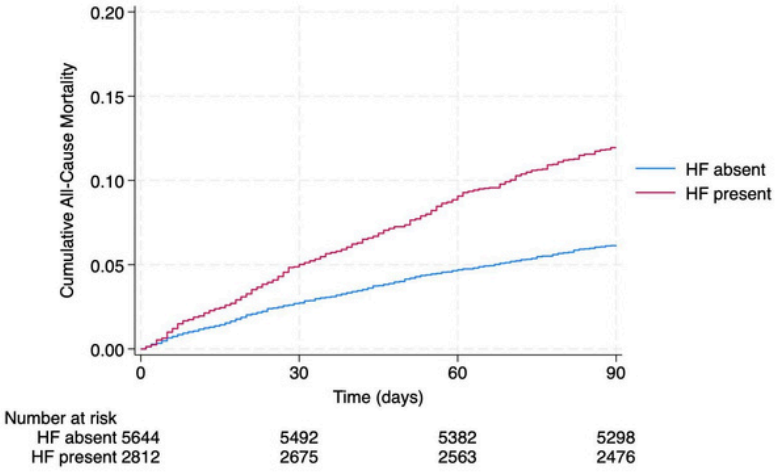


Figure 1B: Kaplan Meier curves for all-cause mortality post-discharge in patients hospitalized for an AECOPD.

The role of early cardiac interventions in improving the clinical trajectories of patients with suspected genetic cardiomyopathies

Chandu Sadasivan, Luke R. Gagnon, Deepan Hazra, Kaiming Wang, Erik Youngson, Jissy Thomas, Anita Y. M. Chan, D. Ian Paterson, Finlay A. McAlister, Tara Dzwiniel, Wayne Tymchak, Susan Christian, Gavin Oudit

Supervisor: Gavin Oudit

INTRODUCTION

Patients with genetic cardiomyopathies experience high morbidity and mortality. Early cardiac interventions and prompt genetic counselling may improve clinical outcomes and prevent progression to advanced heart failure (HF) in this vulnerable patient population.

METHODS

We conducted a prospective cohort study at the multidisciplinary Cardiomyopathy Clinic at the Mazankowski Alberta Heart Institute, including 224 patients with dilated cardiomyopathy (DCM), 72 with hypertrophic cardiomyopathy (HCM), 79 with infiltrative cardiomyopathy (CM), and 46 patients who were stage A/at-risk for genetic cardiomyopathy. A prospective electronic chart review was performed, including patient demographics, medication/device utilization, medical history, genetic testing results, plasma biomarkers (BNP, NT-proBNP, hsTropT), electrocardiogram (ECG), transthoracic echocardiography (TTE), and cardiac magnetic resonance imaging (CMR) data at baseline and follow-up visits.

RESULTS

Pathogenic/likely pathogenic variants were identified in 28.5% of the cohort. This included 33.3% of the DCM cohort (28% TTN mutations) and 34.1% of the HCM cohort (60% MYBPC3 and 20% MYH7). The use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/angiotensin receptor neprilysin inhibitor ($P<0.001$), β-blockers ($P<0.001$), mineralocorticoid receptor antagonists ($P=0.0014$), and sodium/glucose cotransporter-2 inhibitors ($P<0.001$) were all increased at follow-up. Precision-based therapies were also initiated, such as tafamidis for transthyretin amyloidosis (n=21) and enzyme replacement therapy for Fabry disease (n=14). Left ventricular ejection fraction (LVEF) improved from 27% to 43% at follow-up for DCM patients ($P<0.001$) and left ventricular mass index (LVMI) was reduced from 156 g/m2 to 128 g/m2 for HCM patients ($P=0.009$). We also observed reductions in B-type natriuretic peptide ($P=0.048$), N-terminal prohormone of brain natriuretic peptide ($P<0.001$), and high-sensitive troponin T ($P=0.005$) in stage C/HF patients, while stage B/pre-HF patients showed stability in biomarkers. Cardiovascular mortality was low at 1.7% for the entire cohort over a median follow-up of 34 months.

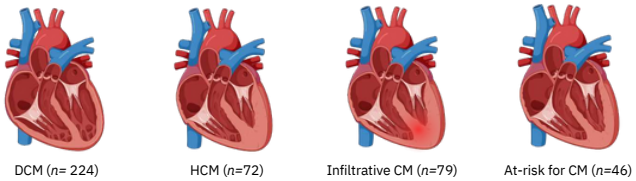
CONCLUSIONS

Multidisciplinary care in a specialized cardiomyopathy clinic can improve the clinical trajectories of patients with genetic cardiomyopathies.

Aims

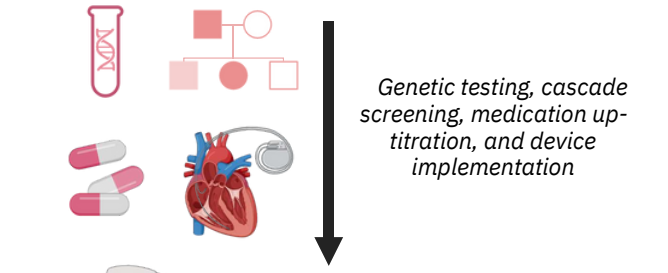
Early cardiac intervention and prompt genetic counselling in patients with suspected genetic cardiomyopathies has the potential to improve outcomes and prevent progression to end-stage heart failure.

Study Design

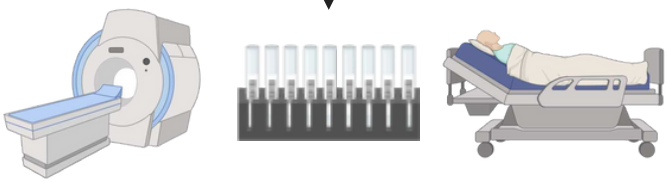


DCM (*n*= 224) HCM (*n*=72) Infiltrative CM (*n*=79) At-risk for CM (*n*=46)

Stage A (*n*=46), Stage B (*n*=187), Stage C (*n*=183), and Stage D (*n*=5)

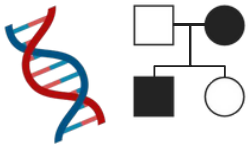


Genetic testing, cascade screening, medication up-titration, and device implementation



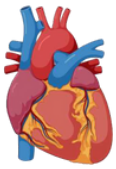
Follow-up imaging (TTE and/or CMR), plasma biomarkers, and clinical outcomes captured at median of 34 months

Results



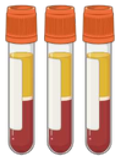
1) Increased genetic testing and cascade screening

28.5% of total cohort with positive genotypes (33.3% of DCM cohort and 34.1% of HCM cohort with testing). 15 patients with FD. 7 patients with hereditary ATTR.



2) Reverse cardiac remodelling

Increased LVEF for DCM patients (27% to 43%, *P*<0.001) and reduction in LVMI for HCM patients (156 g/m2 to 128 g/m2, *P*=0.009).



3) Reduction in plasma biomarkers

Reductions in BNP (*P*=0.048), NT-proBNP (*P*<0.001), and hsTrop (*P*=0.005) were seen in stage C/HF patients, while stage B/pre-HF patients showed stability in biomarkers

4) Favorable clinical outcomes

Stage A/B patients had similar high probability of survival ($\chi 2$=0.204, *P*=0.652). Overall CV mortality rate of 1.7% for the cohort (0.5% for stage B and 3.3% for stage C).

Identifying Patterns of Similarity between Upstream Gene Regions: Insights into Chromatin Organization and Gene Expression Across the Human Genome

Joy Ramielle L. Santos, Weijie Sun, Dominik Cesarz, A. Dean Befus and Marcelo Marcet-Palacios

Supervisor: Marcelo Marcet-Palacios

INTRODUCTION

Upstream gene regions (UGRs) contain regulatory elements important for gene regulation, expression, and chromatin organization. Previously, we conducted an in-depth analysis on the UGRs of preferentially expressed antigen of melanoma family (PRAMEF) genes in chromosome 1 due to the pattern elucidated using our sequence similarity software (SEQSIM). We generated a hypothetical three-dimensional chromatin model. We expand upon this targeted study by exploring UGR patterns across the entire human genome. We aim to identify and catalog all patterns of UGR similarity to investigate whether they hold any significant biological meaning in the future.

METHODS

Our novel software, SEQSIM, was used to generate similarity matrices by comparing 2000 nucleotides upstream of every human gene across chromosomes 1 through 24. Heatmaps were generated for each chromosome and parsed for similarity patterns based on the clear presence of anti-parallel, parallel and checkerboard relationships within the heatmap and involving at least eight genes.

RESULTS

Of the 57245 UGRs analyzed, 6454 (approximately 11% of the genome) exhibited similarity patterns. Despite its small size, chromosome Y (chr24) had the most genes involved in similarity patterns, encompassing 63% of the UGRs on the chromosome. Contrastingly. chromosomes 3, 12, 13, 18 and 20 contained no discernable patterns. We also observed that many of the UGRs involved in patterns were upstream of pseudogenes. In the patterned UGRs, approximately 37% were associated with pseudogenes, higher than the ~24% in the entire genome.

CONCLUSIONS

Our genome-wide analysis of UGRs revealed approximately 11% of UGRs display similarity patterns that could influence genomic architecture and gene regulation mechanisms. Notably, the dense pattern configurations on Chr24 suggest a unique regulatory landscape that warrants further investigation. Additionally, the increased proportion of pseudogene UGRs challenges traditional assumptions about their functionality. These findings suggest new directions for exploring the biological implications of UGRs in gene regulation and expression.

Association between substance use and socioeconomic status using wastewater-based surveillance at eight neighborhoods in an urban center in Alberta, Canada

Navid Sedaghat

Supervisor: Monty Ghosh

INTRODUCTION

The opioid epidemic has become a severe issue in North America. A potential approach to understanding this issue in a comprehensive, and inclusive manner is wastewater-based surveillance (WBS). This study aimed to observe any associations between sociodemographic status (SES) and substance use in communities in an Albertan city.

METHODS

Wastewater was collected three times a week using ISCO 5800 and CEC-A1 autosamplers in eight neighbourhoods. Samples were filtered using a 0.7 µm syringe glass fibre filter, stored at less than 4˚C, and analyzed within three days. Samples were analyzed following direct injection using Agilent 1260 HPLC and Agilent 6460C Triple Quadrupole mass spectrometer (Agilent, Santa Clara, California) for 12 substances and their metabolites. Pearson correlation between sociodemographic indicators and substance consumption (mg/d/1000inh) was calculated using R.

RESULTS

Several correlations were observed in the analysis of 102 samples. Employment percentage correlated strongly with methadone and norfentanyl consumption. Overall, Immigration, education, and median income had low to mediocre correlation with substance use. Correlations between substances were also established. Nicotine correlated strongly with amphetamine, methadone, cocaine, and ethanol. Xylazine was only quantified in the neighbourhood with the lowest SES among the rest. This neighbourhood also had the highest consumption of almost all substances among the rest of the neighbourhoods.

CONCLUSIONS

Analytes of interest were detected and quantified through WBS. The results of this study suggest a more comprehensive approach to harm reduction and possibly more policing to reduce drug dealing, which might decrease substance use in the community and improve individuals' livelihoods. Campaigns and community groups could provide educational materials to inform residents about substance use in their area using data gathered by WBS. WBS can also aid public health officials and policymakers in addressing substance use issues and enable early harm reduction warnings to be issued to health providers and substance users.

p53 associated de novo activation of VWF expression in tumor cells

Noorossadat Seyyedi, Tiffany Lo, Parnian Alavi, Manijeh Pasdar, Nadia Jahroudi

Supervisor: Nadia Jahroudi

INTRODUCTION

Expression of the pro-coagulant protein von Willebrand Factor (VWF) under physiological condition is exclusively restricted to endothelial cells and megakaryocytes. However, its de novo expression is detected in some cancer cells of non-endothelial/megakaryocytic origin and may promote their metastatic potential. p53, a tumor suppressor and a transcription factor, is one of the most frequently mutated genes in cancers. Mutations in p53 lead to dysregulation of p53 target genes expression including NFIB, a major transcriptional repressor of VWF. Previous studies have demonstrated that the dual adhesion and signalling protein plakoglobin can restore tumor suppressor function of mutant p53. We hypothesized that p53 mutations induce de novo activation of VWF, either directly or indirectly through targeting NFIB, while plakoglobin interaction with mutant p53 reverses this effect.

METHODS

H1299, p53 and plakoglobin null non-small cell lung carcinoma cell line was transfected with wild-type-, conformational-, or contact mutant p53, with or without plakoglobin and assessed for VWF and NFIB expression by qRT-PCR, western blot, and immunofluorescence assays. Co-immunoprecipitation analysis was used to determine association of p53 and NFIB. Human Protein Atlas and the TP53 database were surveyed to explore correlation of NFIB and P53 mutation with VWF expression in various cancer cell lines.

RESULTS

We demonstrated that specifically conformational mutant p53 expression in H1299 cells induced VWF expression, downregulated NFIB, and demonstrated NFIB-p53 association. However, plakoglobin co-expression reversed these effects. Database searches demonstrated that 53% of VWF-expressing cells exhibited NFIB downregulating mutations, and amongst the VWF-positive cancer cell lines without NFIB mutation, ~33% expressed p53 conformational mutation.

CONCLUSIONS

Our study revealed a novel mechanism of de novo expression of VWF in cancer cells associated with mutant p53. Downregulation, as well as potentially sequestration/inhibition of NFIB, by mutant p53 could contribute to de novo activation of VWF promoter, while plakoglobin reverses this effect.

The Resilience of a Centralized, Public Health, Tuberculosis Program Performance in Alberta Before and During the Covid-19 Pandemic Disruption

Seun Akinfolarin, Divya Shah, Courtney Heffernan, Tamara Samardzic, Angela Lau, Mary Lou Egedahl, Ryan Cooper, Amy Colquhoun, Stacy Valaire, Alex Doroshenko, Richard Long

Supervisor: Richard Long

INTRODUCTION

Monitoring and evaluation of integrated tuberculosis (TB) services is recommended as a mechanism of accountability, which supports elimination efforts globally. Key TB program performance indicators (KPIs) are described in the latest edition of the Canadian TB standards. The Alberta TB program is carried out via three public health clinics: 1 virtual and 2 outpatient. In this study, we apply these KPIs to Alberta's TB program before and during the COVID-19 pandemic.

METHODS

We obtained TB surveillance data from clinical and public health records pertaining to eight KPIs between January 2018 and May 2022. Then we adjusted entry periods (in months) for each indicator to reflect assessment either before or during the COVID-19 pandemic at its height. We further sub-categorized relevant indicators of program performance by clinic type (virtual or outpatient). Results are expressed as proportions of patients or contacts who satisfied the KPI of interest and shown against the published targets.

RESULTS

KPIs were assessed in two domains: case management and contact management. Overall program performance was good, but slightly below target for four and substantially below target for one KPI. The COVID-19 pandemic had no measurable negative impact on program performance; rather, the performance of three KPIs improved during the pandemic, almost certainly on account of reduced demand – 40% fewer immigration referrals to assess and 55% fewer close contacts of infectious cases.

CONCLUSIONS

The TB program of Alberta was remarkably resilient to COVID-19 pandemic disruptions, in contrast to what has been reported elsewhere in Canada and globally. This is attributed to the organization of the program (it is a centralized public health program with a strong academic collaboration) and a decision to protect TB program staff against Covid-19 secondment. Areas for improvement were identified. The need to streamline data abstraction processes is necessary in the future.

The Resilience of a Centralized, Public Health, Tuberculosis Program Performance in Alberta Before and During the Covid-19 Pandemic Disruption

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Case management KPIs	Target	During pandemic	Post pandemic
HIV tested at diagnosis	>95%	87.0%	85.0%
Timely treatment (within 72hrs of positive NAAT)	>95%	86.7%	89.1%
Early treatment assessment (sputum *and* cxr)	>95%	64.4%	72.8%
Treatment completion	>90%	91.8%	92.4%
Case fatality (all-cause)	<10%	5.8%	7.2%

Contact management KPIs	Target	During pandemic	Post pandemic
Close contacts completely assessed	>95%	81.8%	89.7%
Close contacts starting prevention	>90%	85.4%	88.7%
Close contacts completing prevention	>90%	90.6%	97.0%

Predictors of Diagnostic Delays and Loss to Follow-up in Women with von Willebrand Disease

Jaclyn Shelton, Michelle Millions, Roy Khalife, Linda Sun

Supervisor: Hao Wei (Linda) Sun

INTRODUCTION

Diagnostic delays in von Willebrand disease (vWD) disproportionately affect women. Such delays may lead to poor health outcomes from preventable bleeding complications and increased health resource utilization.

Aims: 1) Examine the prevalence and predictors of diagnostic delays and loss to follow-up in women with vWD. 2) Assess the impact of diagnostic delays on rates of ED visits, red cell transfusions, and hysterectomies.

METHODS

This retrospective cohort study included women ≥18 years with vWD followed by the Northern Alberta Bleeding Disorders Program. Diagnostic delay was determined from the time of first documented bleeding event to the time of vWD diagnosis, with delayed diagnosis defined as >5 years. All bleeding events on the ISTH-BAT were included in the above definition, except for easy bruising. Loss to follow-up was defined as ≥5 years since last hematology visit. Logistic regression was used to assess predictors of diagnostic delays and loss to follow-up.

RESULTS

We included 173 women with vWD. The median age of diagnosis was 27 years (IQR 18-38). The median time from first bleeding symptom to vWD diagnosis was 12.1 years (IQR 4.6-24.2). 73% experienced delayed diagnosis. Compared to women with delayed diagnosis, those diagnosed within 5 years of their first bleeding symptom were more likely to have a known family history of vWD (51% vs 26%, P=0.01).

28% were lost to follow-up for ≥5 years. Only rural residence (OR 1.8, 95% CI 0.9-5.3, P=0.07) trended towards higher odds of loss to follow-up.

Women with diagnostic delays had a significantly higher ISTH-BAT (median 7 vs 5, P=0.005) and higher rates of hysterectomies for heavy menstrual bleeding (HMB; 20% vs 0%, P=0.0006). 17 women underwent surgical procedures for HMB prior to their vWD diagnosis.

CONCLUSIONS

Women with vWD often experienced diagnostic delays and had high rates of loss to follow-up. Alarmingly, the rate of delayed diagnosis was associated with higher rates of surgical interventions for HMB.

Table 1. Characteristics associated with delayed diagnosis of von Willebrand disease.

	Diagnosis <5 years from first symptom (n=41)	Delayed diagnosis >5 years (n=113)	P-value
Rural residence, n (%)	9 (22)	23 (19)	0.91
vWD type, n (%) Type 1 Type 2 Type 3	 30 (73) 7 (17) 2 (5)	 95 (84) 13 (12) 3 (3) 0.35 (0.25-	0.15
Baseline vWF activity, median IU/ml (IQR)	0.31 (0.17-0.38)	0.43) 73/97	0.11
Blood type O, n (%)	21/31 (68)	(75) 7 (5-9) 30	0.33
ISTH-BAT, median (IQR)	5 (4-8)	(26)	0.005
Family history of vWD (prior to patient referral), n (%)	21 (51)		0.01
No family history of vWD or bleeding symptoms, n (%)	7 (17)	28 (25)	0.37
Abnormal INR >1.2 prior to diagnosis, n (%)	0/19 (0)	1/62 (2)	0.61
Abnormal aPTT >38s prior to diagnosis, n (%)	6/20 (30)	13/60 (22)	0.68
Severe bleeding prior to diagnosis (ED visit, hospitalization, transfusions, or surgical hemostasis)	15 (37)	56 (50)	0.21

aPTT, activated partial thromboplastin time; ED, Emergency Department; INR, international normalized ratio; IQR, interquartile range; ISTH-BAT, International Society on Thrombosis and Haemostasis - Bleeding Assessment Tool; vWD, von Willebrand disease; vWF, von Willebrand factor.

Table 2. Association between diagnostic delays and gynecological outcomes.

	Diagnosis <5 years from first symptom (n=41)	Delayed diagnosis >5 years (n=113)	P-value
Hysterectomy, n (%)	0 (0)	23 (20)	0.0006
HMB requiring D&C, n (%)	1 (2)	13 (12)	0.11
HMB requiring endometrial ablation, n (%)	2 (5)	13 (12)	0.36
HMB requiring ED visits, n (%)	9 (22)	18 (16)	0.53
HMB requiring red cell transfusions, n (%)	5 (12)	8 (7)	0.33
Severe PPH, n (%)	1 (2)	12 (11)	0.19

D&C, dilatation and curettage; ED, Emergency Department; HMB, heavy menstrual bleeding; PPH, postpartum hemorrhage.

Sex, ethnicity and clinical outcomes in autoimmune hepatitis: results from a large multicenter longitudinal cohort

Lytvyak E, Shreekumar D, Hirschfield GM, Plagiannakos CG, Ko HH, Swain M, Hercun J, Worobetz L, Vincent C, Flemming J, Qumosani KM, Chen T, Grbic D, Cheung A, Umar N, Iqbal I, Gulamhusein AF, Mason AL, Hansen BE, Montano-Loza AJ

Supervisor: Ellina Lytvyak

INTRODUCTION

We aimed to identify and quantify the magnitude of associations between sex, ethnicity, treatment response and clinical outcomes in a large multicentric cohort of people with autoimmune hepatitis (AIH) across Canada.

METHODS

A retro- and prospective cohort study was conducted using data from the Canadian Network for Autoimmune Liver Diseases (CaNAL). Adverse events were defined as the development of decompensation, hepatocellular carcinoma (HCC), liver transplantation (LT), or death. Treatment response was defined as normalization of alanine transaminase 6 months post-treatment initiation.

RESULTS

Data of 1198 people with AIH with 13443 person-years follow-up were analyzed. No significant difference was observed between sexes in the frequency of cirrhosis, decompensation and mortality. However, males had a higher frequency of HCC and LT compared to females as well as poorer transplant-free survival. Males have substantially lower biochemical treatment response than females.

Compared to other ethnicities, Indigenous Canadians had the highest frequency of adverse events (44.1% vs. 27.0%; p=0.027) that was mainly driven by twice the frequencies of development of decompensation, LT, mortality and poorer transplant-free survival. They also had a substantially shorter event-free survival time (4.3 [IQR 1.5–9.5] vs. 8.2 [IQR 3.8–14.2] years; p<0.001).

In a time-dependent Cox regression, Indigenous people have a significantly higher risk of developing adverse outcomes (HR 2.70, 95%CI 1.60–4.54; p<0.001) that remained strong after adjusting for male sex, age and cirrhosis at diagnosis and lack of treatment response (HR 2.80, 95%CI 1.01–7.80; p=0.049).

CONCLUSIONS

Males living with AIH have a higher frequency of HCC and LT and have lower rates of treatment response compared to females. Indigenous Canadians living with AIH have a substantially higher risk of developing adverse liver outcomes compared to other ethnic groups.

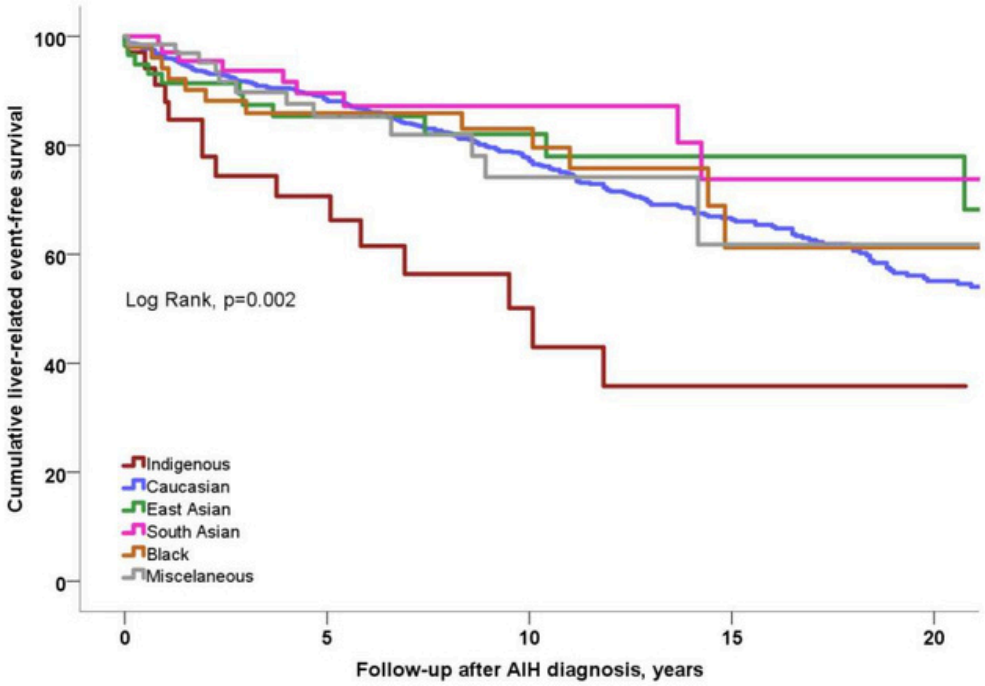


Figure 1. Unadjusted cumulative liver-related event–free survival over time, by ethnicity. Adverse events include development of decompensation, hepatocellular carcinoma (HCC), liver transplantation (LT), or death.

Using a Shared Infusion Clinic for Outpatient Management of Sickle Cell Vaso-occlusive Crisis as a Strategy of Decreasing Emergency Department Visits

Melissa Shyian, Lauren Bolster

Supervisor: Lauren Bolster

INTRODUCTION

Complications of sickle cell disease (SCD), including vaso-occlusive crises (VOC), often require emergency room visits or hospitalization for management. Patients followed by the Edmonton Hemoglobinopathy Clinic experiencing early VOC symptoms can alternatively present to the Medical Outpatient Unit (MOU) to be assessed and receive treatment from their personalized pain plan. This study retrospectively evaluated the outcomes of this treatment strategy to assess patients and provide appropriate treatment, thereby reducing the frequency of ED presentations for SCD patients.

METHODS

Chart review of patients 18 years or older with SCD who presented to MOU from November 2019 to December 2022 for management of VOC was completed. Encounters within 7 days were counted as one episode and assumed to be the same VOC event.

RESULTS

Twenty-six SCD patients had at least one MOU encounter for VOC with a total of 136 encounters (median 2, maximum 25), accounting for 96 separate episodes of VOC (median 2, maximum 19). IV fluids were administered in 129 encounters (95%), and pain medications were given 64 encounters (47%). 109 encounters had assessment by nurse only (80%). Patients were discharged home in 134 of 136 encounters (99%), with only 2 encounters requiring assessment in ED. Seventy of 96 episodes of VOC treated in MOU did not have presentation to ED within 30 days (73%). Total ED visits for this cohort decreased from 59 in 2016-2018 to 38 during the time of this study.

CONCLUSIONS

Treatment of VOC in an outpatient setting for assessment and treatment was associated with a decreased number of ED visits in our cohort.

New and persistent psychoactive medication use in intensive care unit survivors with COVID-19

Andrea C Shysh, Finlay A McAlister, Luan Manh Chu, Jason Weatherald, Sean M Bagshaw, Ken Kuljit S Parhar, Fernando G Zampieri, Jacob C Jentzer, Erik Youngson, Sameer S Kadri, Padma Kaul, Sean van Diepen

Supervisor: Sean van Diepen

INTRODUCTION

COVID-19 intensive care unit (ICU) survivors may have higher rates of post-intensive care syndrome. Our objective was to determine the frequency and predictors of new psychoactive medication prescriptions at hospital discharge in COVID-19 ICU survivors and to describe the associated one-year clinical outcomes.

METHODS

This is a retrospective, population-based cohort study. Sedative-naïve adults, no psychoactive medication filled 6 months prior to hospitalization, who were admitted to an ICU with a COVID-19 diagnosis and survived to hospital discharge between January 1, 2021 and July 31, 2022 were included. New psychoactive medication recipients were identified at discharge and persistent recipients after one year. Multivariable regression identified factors associated with new psychoactive use and the association with one-year all-cause mortality, hospital readmission, and emergency room (ER) visits.

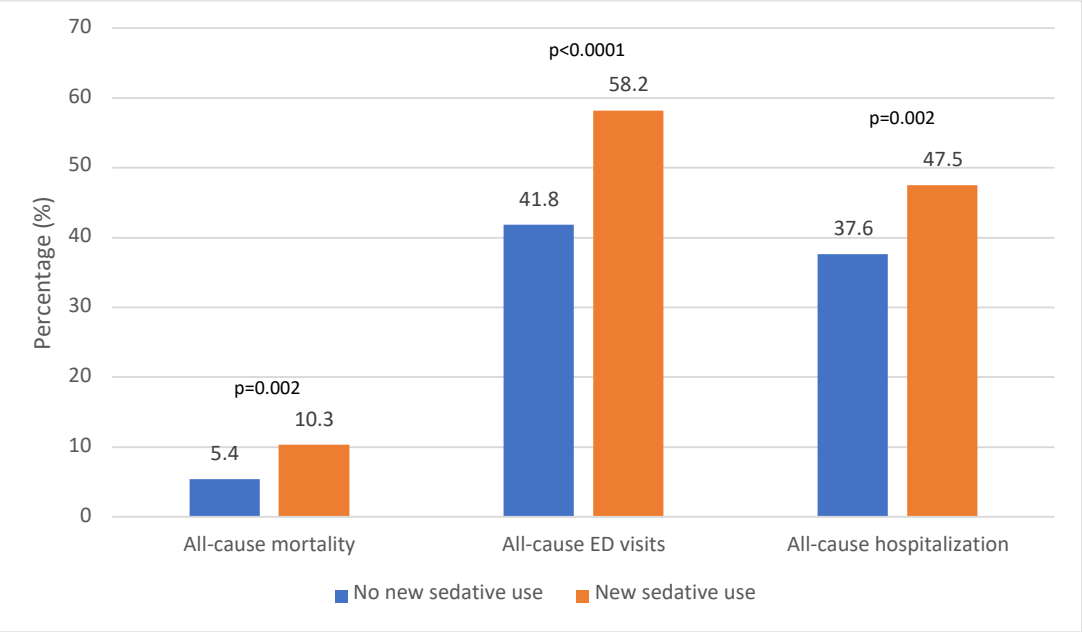
RESULTS

Among 1,486 psychoactive-naïve adults (mean 56 years, 67.5% male) who survived an ICU stay with COVID-19 (mean ICU length of stay [LOS] 6.6 days, mean hospital LOS 17.1 days), 261 (17.6%) filled psychoactive medications at hospital discharge. Common prescriptions included benzodiazepines (41%), opioids (28.3%), anti-psychotics (20.3%), and selective serotonin reuptake inhibitors (15.0%). At one year, 135 (51.7% of new recipients) had persistent medication dispensations. Independent predictors of new psychoactive prescriptions included pre-admission diagnosis of anxiety (adjusted Odds Ratio [aOR] 3.40; 95% CI 1.62-7.12), rural residence (aOR 1.48; 95% CI 1.06-2.05), and hospital LOS (aOR 1.01; 95% CI 1.00-1.01). Patients with new discharge prescriptions had higher one-year all-cause mortality (10.3% vs. 5.4%, aOR 2.26, 95% CI 1.01-5.07) and ER visits (58.2% vs. 41.8%, aOR 1.66, 95% CI 1.14-2.41).

CONCLUSIONS

New psychoactive medications were common in COVID-19 ICU survivors and approximately half of patients were still receiving medications one-year later. Our finding that new post-discharge psychoactive medications were associated with a higher risk of mortality and ER visitation suggests the need to reassess medication appropriateness before or at discharge.

Figure 1. One-year outcomes after index hospital discharge in COVID-19 ICU survivors, stratified by new psychoactive use at the time of index hospital discharge.



Abbreviations: ICU, intensive care unit; ED, emergency department.

Binding Hepatitis B virus’ chronic form by targeting its pre-core promoter G-quadruplex

Jessica Skoreyko, Emma Kasinyabo, Kira Sviderskaia, Hoa Le, Vannessa Meier-Stephenson

Supervisor: Vanessa Meier-Stephenson

INTRODUCTION

Hepatitis B Virus (HBV) remains chronic due to the covalently closed circular DNA (cccDNA) template that hides away in the nucleus and is untargeted by the immune system. Current therapeutics can decrease viral loads by targeting pathways downstream of this cccDNA but are unable to clear this stable viral template. If we want to target chronic HBV, it will be necessary to target the cccDNA. Interestingly, there is a highly conserved non-conical structure of DNA, known as a G-quadruplex (GQ) within the precore promoter region of the cccDNA, that is central to viral transcription. We hypothesize that the use of known GQ-binding drugs, developed in the anti-cancer realm, can bind and potentially interfere with HBV’s GQ and directly reduce viral transcripts and proteins.

METHODS

Using HepG2-NTCP cells, alamarBlue viability assays were performed to assess for toxicities of the GQ-binding drugs. Cells were then plated and infected with HepAD38-derived virus at 2000 genome equivalents/cell. GQ-binding drugs were then added 1dpi. At 4dpi and 7dpi, the cells were harvested and assessed for markers of infection (pgRNA, total HBV DNA, HBsAg). A subset of cells was fixed and imaged for HBV core protein to confirm the degree of infection.

RESULTS

Viability assays confirm the concentrations of the GQ-binding drugs used. Microscopy confirmed ~15% infection 7dpi (typical for the field). Preliminary data suggest that GQ-binding drugs result in decreased pgRNA and total HBV DNA, as well as reduced viral core protein output.

CONCLUSIONS

GQ-binding drugs appear to be a promising therapeutic against HBV. Future experiments include replicating previous findings in primary human hepatocytes along with testing of novel therapeutic inventions from our lab.

Transcriptomic Feature Importance Analysis for Treatment Response in Primary Biliary Cholangitis using Machine-Learning

Hussain Syed, Cassaday Allers, Sandra O'Keefe, Doaa Waly, Andrew Mason

Supervisor: Andrew Mason

INTRODUCTION

Prognosis in Primary Biliary Cholangitis (PBC) may be determined by non-survival-based criteria, such as the POISE clinical trial endpoint, which includes reduction of alkaline phosphatase < 200 IU and normalization of bilirubin. These criteria challenge traditional transcriptomic tools, which struggle to identify complex factors determining response or non-response in patient cohorts. To overcome this, we employed machine learning to extract features relevant to patient response.

METHODS

Whole-blood RNA-seq data from 88 baseline and 53 post-treatment samples of PBC patients from the POISE study was subjected to recursive feature elimination with Logistic Regression to identify genes relevant to response to obeticholic acid. Support vector machine learning was used to model the post-treatment dataset which was validated against the baseline dataset to predict patient response based on the POISE criteria. The top 1000 features were extracted for pathway analysis.

RESULTS

The SVM model predicted pre-treatment response (AUROC=0.86), whereas levels of alkaline phosphatase (AUROC=0.82), and bilirubin (AUROC=0.64) were less predictive. Pathway analysis on the top 1000 features identified dysregulated pathways: (i) TP53 network linked with DNA damage, (ii) NRF2 pathway associated with generation of reactive oxygen species (ROS), (iii) chemokine signaling and prostaglandin and leukotriene metabolism consistent with cellular senescence, (iv) epithelial to mesenchymal transition, and (v) PI3K Akt mTOR signaling reflecting metabolic remodeling.

CONCLUSIONS

The analyses revealed transcriptional activation of pathways previously described in damaged biliary epithelial cells (BEC), reflecting the systemic nature of disease. The analyses also uncovered potentially novel pathways we have recently described in BEC including mitochondrial dysfunction linked with antimitochondrial antibody formation associated with DNA damage, ROS and metabolic remodeling with PI3K/Akt/mTOR signaling. BEC from PBC patients express cellular senescence markers with abnormal autophagy and epithelial to mesenchymal transition which were also observed to be activated in whole blood. Further investigation into these pathways may improve our understanding of PBC pathogenesis.

Tumour Secreted Inosine and Hypoxanthine Promote RBFOX1 Degradation, Cardiomyocyte Dedifferentiation and Susceptibility to Cardiotoxicity

Saymon Tejay, Maria Areli Lorenzana-Carillo, Yuan Yuan Zhao, Farah Eaton, Michelle Mendiola Pla, Dawn E Bowles, Ian D Patterson, Edith Pituskin, John R Ussher, Evangelos Michelakis and Gopinath Sutendra

Supervisor: Gopinath Sutendra

INTRODUCTION

It is well established that cancer cells can secrete numerous signalling factors that affect distant normal tissues such as skeletal muscle or adipose tissue break down by tumour necrosis factor (TNFa) and lipid mobilizing factor (LMF) respectively. What remains unclear is if tumour secreted factors (TSFs) can initiate a signalling cascade in cardiomyocytes to render these cells more susceptible to cell death and cardiotoxicity after DNA damaging chemotherapy treatment, a common adverse side effect.

METHODS

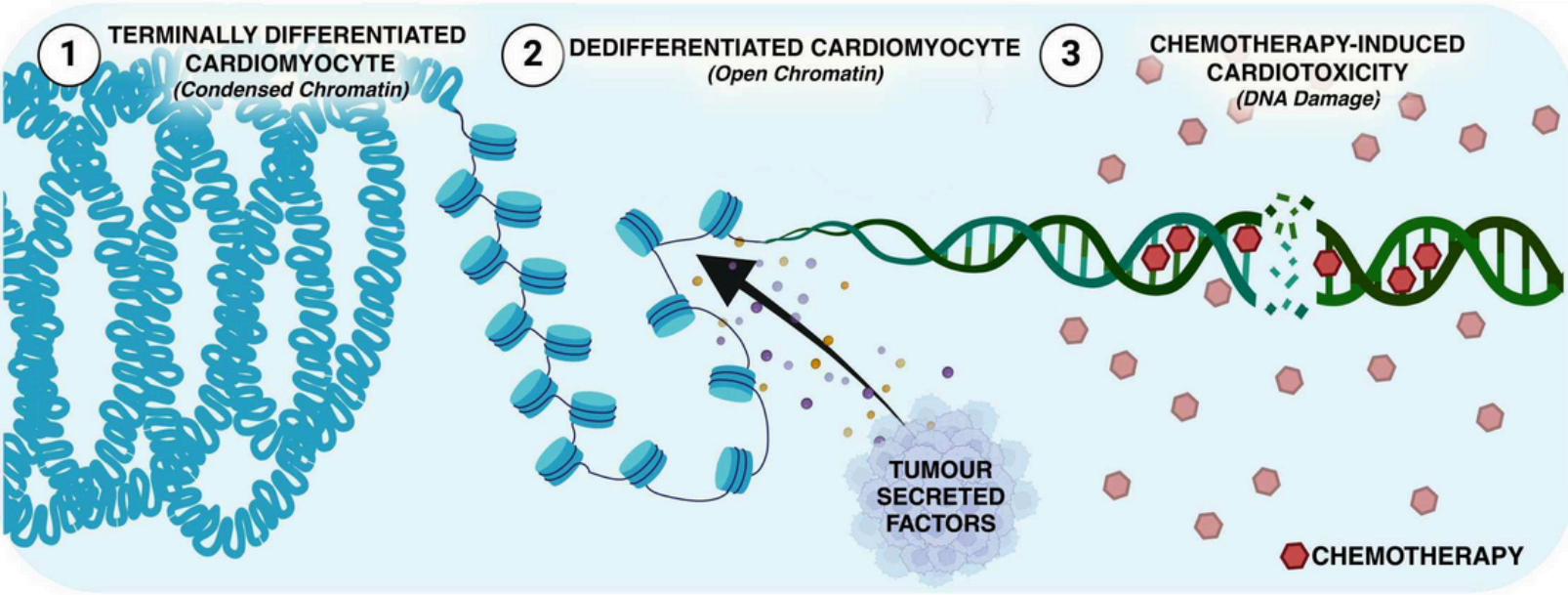
Clinically relevant tumour xenotransplant mice were used to identify TSFs in the serum and their effect on the myocardium. Serum and tumour biopsies were collected from breast cancer patients prior to treatment and development of cardiotoxicity. We generated cardiomyocyte-specific RBFOX1-deficient mice and assessed myocardial signalling and heart function (via echocardiography) prior to and after chemotherapy (anthracycline) treatment. Human chemotherapy induced cardiotoxicity myocardial biopsies were used to translate mechanistic findings.

RESULTS

We found that tumour secreted inosine and hypoxanthine were significantly elevated in the serum of lung cancer mice and breast cancer patients that developed cardiotoxicity. Mechanistically, we found that tumour secreted inosine and hypoxanthine can bind and activate the A2A receptor on cardiomyocytes, activating CAMKIIδ, which phosphorylates the postnatal mRNA splicing factor RBFOX1 on threonine-197, resulting in its caspase-dependent degradation. Loss of RBFOX1 initiates cardiomyocyte dedifferentiation and epigenetic remodeling, promoting a more open chromatin state and accessible chromatin that increases susceptibility to DNA damage and cell death when treated with DNA damaging or intercalating anticancer agents. RBFOX1- deficient male and female mice develop significant cardiotoxicity when treated with low dose doxorubicin (commonly used DNA intercalating chemotherapy). RBFOX1 loss correlated with cell death markers (P53, cleaved caspase 9) in anthracycline-mediated cardiotoxicity patients.

CONCLUSIONS

This work identified a potential biomarker (i.e. inosine/ hypoxanthine) and mechanism for susceptibility to cardiotoxic anti-cancer drugs in preclinical models and patients.


1
TERMINALLY DIFFERENTIATED CARDIOMYOCYTE
(Condensed Chromatin)
2
DEDIFFERENTIATED CARDIOMYOCYTE
(Open Chromatin)
3
CHEMOTHERAPY-INDUCED CARDIOTOXICITY
(DNA Damage)
TUMOUR SECRETED FACTORS
CHEMOTHERAPY

Liver stiffness measurement by vibration-controlled transient elastography predicts adverse clinical outcomes in autoimmune hepatitis: results from a large multicenter longitudinal study

Narmeen Umar, Ellina Lytvyak, Gideon M. Hirschfield, Christina Plagiannakos, Hin Hin Ko, Mark G Swain, Julian Hercun, Lawrence Worobetz, Catherine Vincent, Jennifer Flemming, Karim Qumosani, Tianyan Chen, Dusanka Grbic, Angela Cheung, Aldo Montano-Loza

Supervisor: Aldo Montano-Loza

INTRODUCTION

Non-invasive techniques may have potential to predict disease outcomes and evaluate the effectiveness of therapies in people with autoimmune hepatitis (AIH). We aimed to investigate the usefulness of liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) in predicting clinical outcomes in a large cohort of people with AIH across Canada.

METHODS

We conducted a multicenter, retro- and prospective cohort study of people with AIH from the Canadian Network for Autoimmune Liver Diseases (CaNAL) registry. Inclusion criteria were a simplified AIH score ≥ 6 and at least one reliable LSM by VCTE performed before adverse events. The primary endpoint was the occurrence of adverse liver outcomes (decompensation, hepatocellular carcinoma (HCC), liver transplantation (LT) or death). Treatment response was defined as the normalization of ALT at 6 months after treatment initiation.

RESULTS

We evaluated 853 people with AIH (73.8% females, 74.5% Caucasians, median age at diagnosis of 45.9 years) with 8394 person-years follow-up. The first VCTE was performed at median of 41.2 months after the AIH diagnosis, and median LSM value was 8.7 kPa. The LSM was strongly associated with development of adverse outcomes. In time-dependent multivariable Cox regression analysis, after adjustment for male sex, age at diagnosis, cirrhosis at diagnosis and lack of biochemical treatment response, LSM was independently associated with adverse outcomes. Based on LSM value, people were stratified into low (< 8.0 kPa), medium (8.0 – 13.9 kPa) and high-risk (≥ 14.0 kPa) groups. In comparison to low-risk (reference) group, medium-risk group had four-fold and high-risk group had over ten-fold risk of adverse outcomes.

CONCLUSIONS

LSM by VCTE is strong independent predictor for adverse liver outcomes in people with AIH when considering risk factors and biochemical treatment response. LSM values by VCTE might help to establish risk stratification to identify people with AIH who may benefit from screening for liver decompensation, HCC, and timely LT referral.

Figure 1a

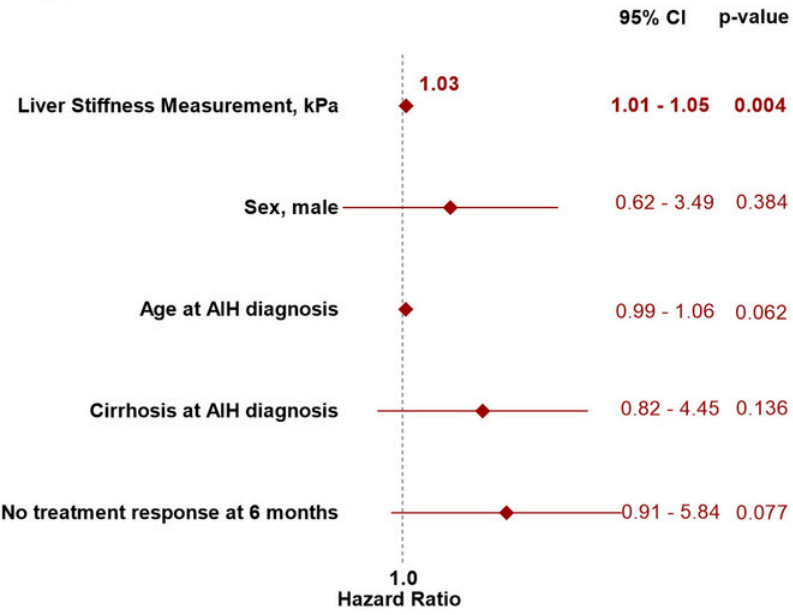
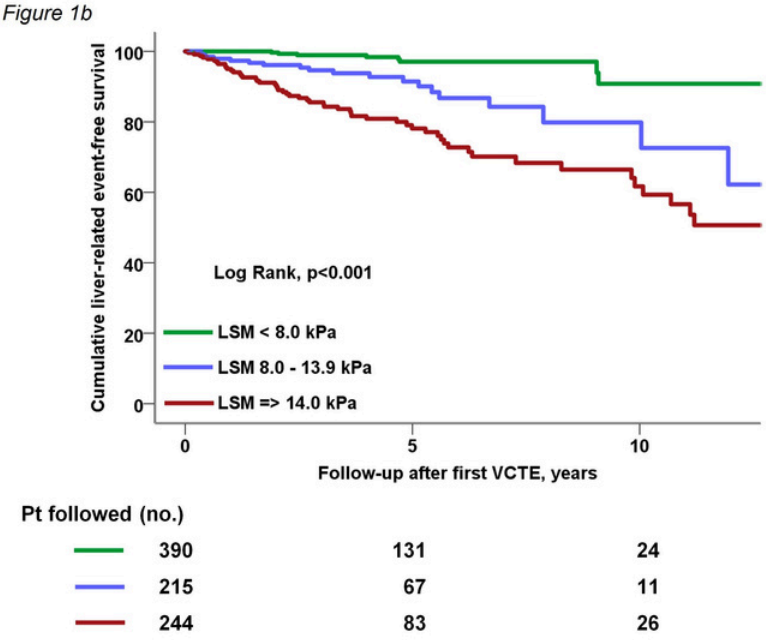


Figure 1b



Pt followed (no.)

LSM < 8.0 kPa	390	131	24
LSM 8.0 - 13.9 kPa	215	67	11
LSM => 14.0 kPa	244	83	26

Advanced Age Considerations in Randomized Clinical Trials of Adults Receiving Maintenance Dialysis: A Meta-Epidemiologic Study

Kevin Wang, Zoe Bamber, Scott Klarenbach, David Collister

Supervisor: David Collister

INTRODUCTION

Randomized controlled trials (RCTs) are essential to inform clinical practice but may lack external validity due to stringent eligibility criteria. Age is an important factor in many chronic diseases including kidney failure and may influence adherence, outcomes and competing risks. Given the aging dialysis population globally, we sought to characterize how age was incorporated in the design and conduct of contemporary RCTs in dialysis.

METHODS

We searched PubMed for RCTs published in high-impact general medicine journals, nephology journals and cardiology journals that specifically recruited adults with kidney failure being treated with either maintenance dialysis or peritoneal dialysis (but not kidney transplantation). Information related to study characteristics, such as study design, population, inclusion/exclusion criteria, intervention, outcomes and age-related factors were abstracted independently by two reviewers.

RESULTS

Among 561 included RCTs, 69.7% were parallel and 28.0% were crossover in design; and 80.6% were conducted in the hemodialysis population. The median size was 60 (IQR, 26-151) participants, and the median follow-up period was 154 (IQR, 42-365) days. The mean age was 58.47 (SD 6.56). Trial characteristics independently associated with mean age were PD trials; and cardiovascular, hemodialysis, antibiotic, anticoagulant and vascular assess interventions. In terms of trial design, 17.1% of RCTs had an upper age limit for eligibility with the most common cutoffs being 75 (4%), 80 (8%) and 85 (2.5%) years. Exclusion for age-related comorbidities was not uncommon including cognitive impairment (n=51, 9.2%), frailty (n=4, 0.7%), long term care (n=5, 0.9%) and visual/hearing impairment (n=14, 2.5%)

CONCLUSIONS

RCTs in dialysis are not representative of the general dialysis population with regards to age and this is in part due to the possible in appropriate exclusion of elderly participants. It is important that the elderly are represented in RCTs in dialysis so that their results are applicable to the aging dialysis population.

Validation of Emergency Medical Services Administrative Codes to Identify an Out-of-Hospital Cardiac Arrest Cohort

Si Cong Ye MD MHSc; Ian Blanchard PhD; Qiuli Duan MSc; Ting Wang MMath; Xiaoming Wang PhD; Jeffrey Bakal PhD; Christopher B. Fordyce MD; Brian Grunau MD; Julie Kromm MD; Padma Kaul PhD; Sean van Diepen MD MSc

Supervisor: Sean van Diepen

INTRODUCTION

Prospective out-of-hospital cardiac arrest (OHCA) registries are limited to regional Emergency Medical Services (EMS) datasets in major urban locations and are resource-intensive to maintain with manual record review. Thus, the ability to accurately identify EMS-treated OHCA from population-based administrative data may potentially provide a more accurate representation of OHCA epidemiology and outcomes.

METHODS

The study included all adults ≥18 years evaluated by EMS personnel and flagged for suspected OHCA in Edmonton and Calgary between 2018-2020. The Alberta EMS dataset captures data from all provincial EMS encounters, including administrative codes for cardiac arrest characteristics, on-scene treatment, and clinical outcomes. Candidate codes of interest were selected based on plausible clinical association with OHCA. Suspected OHCA encounters were linked to the Canadian Resuscitation Outcomes Consortium (CanROC) cohort, a gold standard reference cohort developed through chart abstraction by research paramedics to meet a standardized definition for non-traumatic OHCA requiring: (1) defibrillation by bystander or EMS-applied automated external defibrillators; or (2) EMS-performed chest compressions. The analysis identified individual or combinations of codes with ≥80% specificity for confirmed non-traumatic OHCA.

RESULTS

Among 14,451 EMS encounters with suspected OHCA, 8524 were confirmed to have non-traumatic OHCA. Individual codes that had ≥80% specificity for non-traumatic OHCA included bystander cardiopulmonary resuscitation (specificity 99%; sensitivity 0.06%), electrical therapy (specificity 99%; sensitivity 6%), mechanical ventilation (specificity 99%; sensitivity 0.02%), and return-of-spontaneous-circulation at emergency department arrival (specificity 89%; sensitivity 10%). Combining codes in pairs identified an additional 17 combinations above the specificity threshold, though sensitivity was poor overall (Table 1).

CONCLUSIONS

In an analysis of a population administrative dataset, we identified 21 individual and combinations of EMS codes that had high specificity for identifying non-traumatic OHCAs. These findings could be leveraged to develop pre-hospital OHCA cohorts suitable for future quality assurance or research efforts.

Table 1: Performance of EMS Administrative Codes Meeting ≥80% Specificity for Non-Traumatic Out-of-Hospital Cardiac Arrest

EMS Codes	Specificity	Sensitivity	PPV	NPV
Individual Codes				
Bystander CPR	0.99	0.0006	0.23	0.41
Electrical therapy	0.99	0.06	0.40	0.41
Mechanical Ventilation	0.99	0.0002	0.05	0.41
ROSC at ED arrival	0.89	0.10	0.57	0.41
Code Combinations				
EMS Shock and King Laryngeal Tube Airway	0.92	0.06	0.53	0.41
EMS Shock and Cardiac Arrest at Primary Impression	0.91	0.09	0.58	0.40
EMS Shock and EMS Epinephrine	0.90	0.10	0.57	0.41
EMS Shock and Advanced Airway	0.90	0.09	0.56	0.41
EMS Shock and Bag-Valve Mask	0.90	0.09	0.56	0.41
EMS Shock and Witnessed Arrest	0.90	0.08	0.54	0.40
EMS Shock and Drug Therapy	0.88	0.10	0.55	0.41
EMS Shock and EMS CPR	0.87	0.10	0.53	0.40
Witnessed Arrest and King Laryngeal Tube airway	0.86	0.12	0.55	0.40
Cardiac Arrest at Primary Impression and King Laryngeal Tube airway	0.84 0.82	0.15 0.16	0.58 0.56	0.41 0.40
King Laryngeal Tube airway and Bag-Valve Mask	0.81 0.81	0.19 0.18	0.58 0.57	0.41 0.41
EMS Epinephrine and King Laryngeal Tube airway	0.81 0.80	0.16 0.21	0.54 0.60	0.40 0.41
Witnessed Arrest and Advanced Airway	0.80	0.19	0.59	0.41
EMS CPR and King Laryngeal Tube Airway	0.80	0.19	0.58	0.41
Cardiac Arrest at Primary Impression and Advanced Airway				
Witnessed Arrest and EMS Epinephrine				
Drug Therapy and King Laryngeal Tube Airway				

Abbreviations: CPR – Cardiopulmonary resuscitation; ED – Emergency department; EMS – Emergency medical services; NPV – Negative predictive value; PPV – Positive predictive value; ROSC – Return of spontaneous circulation

A critical contribution of cardiac myofibroblasts and a predictive role of UCP2 SNPs for right ventricular decompensation and CHF

Yongneng Zhang, Alois Haromy, Yongsheng Liu, Yuanyuan Zhao, Gopinath Sutendra, Evangelos D. Michelakis

Supervisor: Evangelos D. Michelakis

INTRODUCTION

The mechanism of transition from compensated (cRVH) to decompensated right ventricular hypertrophy (dRVH) is unknown. We hypothesized that a transition from cardiac fibroblasts (cFB) to cardiac myofibroblasts (cMFB) underlies this mechanism. Decreased cFB mitochondrial calcium (mCa++) promotes transition to cMFB through methylation of MICU1 and lack of UCP2 (both components of the mCa ++ uniporter). The loss-of-function UCP2 SNP rs659366 has also been linked with worse outcomes in pulmonary hypertension (PHT).

METHODS

We studied RVs from a monocrotaline-rat PHT model, separating cRVH from dRVH by catheterization and Echo criteria; We measured RV pressure in isolated perfused hearts and sarcomere shortening in isolated RV cardiomyocytes; and studied human RVs in a cohort of 72 patients with both heart tissues and clinical data.

RESULTS

In isolated hearts, RV systolic pressure was lower in dRVH but in isolated cardiomyocytes (CM), contractility was not, pointing to a non-cardiomyocyte cause. The number of cMFB was dramatically increased in dRVH compared to Control and cRVH. mCa++ was progressively decreased from Control to cRVH to dRVH c(M)FB, while it was not different in CM. The MICU1 methyltransferase PRMT1 and MICU1 methylation were increased but the expression of UCP2 was decreased from Control to cRVH to dRVH cMFB (but not CM). In human RVs, dRVH had increased number of cMFB compared to Control and cRVH. Cytoplasmic PRMT1 was increased and UCP2 was decreased from Control to cRVH to dRVH c(M)FB. The presence of rs659366 UCP2 SNP was associated with decreased TAPSE and cardiac index compared to non-carriers with similar PA pressures.

CONCLUSIONS

A change of cell identity (cFB to cMFB) in the RV may drive dRVH, rather than contractile failure. UCP2 SNPs (which can be detected in the blood) may predict early dRVH, improving patient management since the transition from cRVH to dRVH can occur much faster than in the left ventricle.

Quality Improvement Abstracts

Improving Patient Outcomes in the Vulvar Dermatology Clinic

Kaylin Bechard, Anita Truong, Samuel Lowe, Pamela Mathura, Reidar Hagtvedt, Marlene Dytoc

Supervisor: Marlene Dytoc

INTRODUCTION

The prevalence of vulvar disease is underestimated and has a significant impact on quality of life. The validated Vulvar Quality of Life Index (VQLI) was applied at baseline and follow-up for vulvar dermatology consults to better understand the impact of vulvar disease on overall health and improve patient-centered care.

METHODS

Randomized controlled clinical trial was completed with two patient cohorts, intervention, completing a baseline and follow-up VQLI, and control, completing a follow-up VQLI. As a primary outcome, follow-up VQLI scores were compared. Secondary outcomes included treatment adherence; self-reported wellbeing, symptom improvement, whether their health-related concerns were addressed; comparing baseline and follow-up VQLI scores within the intervention group. Data were analyzed, expressed as mean and confidence interval. The primary outcome was analyzed using student t-tests and Fisher's exact test. P-values < 0.05 were considered statically significant.

RESULTS

42 participants were included (23 intervention, 19 control). There was a significant difference (unequal t-test p-value <0.0001) between baseline and follow-up VQLI amongst the intervention group, mean VQLI 18 [6, 36] and 8.3 [0, 18]. Mean follow up VQLI scores in the intervention were lower versus the control group, 8.3 [0, 18] and 12.8 [0, 38], but not statistically significant (unequal t-test p-value 0.1529). There was a significant difference in patient self-reported wellbeing ($p=0.017$), but not in symptom improvement ($p = 0.684$), nor whether their health-related concerns were addressed ($p = 0.391$). Treatment adherence between the cohorts was statistically similar ($p= 0.428$).

CONCLUSIONS

The VQLI scores between cohorts at follow-up assessments was statistically similar. This may be due to sample size, lack of comparison of the change in VQLI scores between the groups, current comprehensive global assessment in the clinic. There was a significant difference in patient-reported wellbeing. Treatment adherence, improvement of symptoms and whether patients felt their health-related concerns were addressed were statistically similar.

COMPETENCY BASED MEDICAL EDUCATION: O-SCORE CHARACTERISTICS OF PROCEDURAL AND COGNITIVE ASSESSMENTS IN GASTROENTEROLOGY RESIDENCY TRAINING

Jared Cooper, Michal Gozdzik, Hollis Lai, Jason Silverman, Karen I. Kroeker

Supervisor: Karen Kroeker

INTRODUCTION

Competence By Design (CBD) assesses a physician trainee's ability to demonstrate competence in CanMEDS roles via entrustable professional activities (EPAs). EPAs utilize the O-SCORE as the metric for assessing competence. This score was developed and validated for surgical/procedural subspecialties; however, CBD currently coopts this scale for both procedural and non-procedural (cognitive) EPAs. Our study aims to assess for differences in O-SCORE utilization between cognitive and procedural EPAs.

METHODS

Anonymized data for all Adult GI subspecialty EPAs completed from Jun 2019 to Jan 2023 at the University of Alberta was obtained. Evaluator sex, clinical vs academic practice, advanced training expertise, and EPA score was extracted. Locally a score of 5 denotes competence, while a 1-3 indicates competence was not yet achieved. A score of 4 may be accepted as evidence of competence (neutral score), at the discretion of the local competency committee. Data was analyzed via T-tests and ANOVA with 95% confidence intervals (CI). A p-value of <0.05 was significant.

RESULTS

2264 EPAs were assessed including 1385 cognitive and 879 procedural EPAs. The number of EPAs completed by evaluators ranged from 11 to 165 with a mean of 60 (standard deviation: 40). Results of O-SCORE usage is summarized in Figure 1A-B. The majority of EPAs indicate competence, with 20-25% neutral, and <10% did not achieve competence. Less than one of third of evaluators utilized a score of 1 or 2 across all EPAs, and zero evaluators utilized a score of 1 for cognitive EPAs. Most commonly evaluators to utilized 3/5 options of the O-SCORE. Separated by EPA type, it was most common to utilize 2/5 and 4/5 options for cognitive and procedural EPAs respectively.

CONCLUSIONS

Across total, cognitive, and procedural EPAs there are low rates in the utilization of the whole O-SCORE scale, and our study highlights a discrepancy between procedural and cognitive EPAs.

Figure 1. A) Number and proportion of Entrustable Professional Activities (EPA) stratified by type and competence evaluation. **B)** Number and proportion of Entrustable Professional Activities (EPA) stratified by type with scored 1-5 and percent (%) of staff utilizing each score stratified by EPA type **C)** Number, mean, and mean difference of Entrustable Professional Activities (EPA) stratified by evaluator sex and EPA type. **D)** Number, mean, and mean difference of Entrustable Professional Activities (EPA) stratified by evaluator academic vs clinical status and EPA type. **E)** Number, mean, and mean difference of Entrustable Professional Activities (EPA) stratified by evaluator advanced training and EPA type. CI: Confidence interval; SD: standard deviation; *: p<0.05

A)

	Competence Evaluation	Number	%
Total	Achieved	1852	69.7
	Neutral	613	23.0
	Not Achieved	195	7.3
Cognitive	Achieved	1041	75.2
	Neutral	282	20.3
	Not Achieved	63	5.5
Procedural	Achieved	811	63.6
	Neutral	332	26.0
	Not Achieved	132	10.3

B)

	EPA Score	Number	Percent	% Staff Utilizing
Total	1	22	0.8	29
	2	17	0.7	27
	3	156	5.9	67
	4	613	23.0	96
	5	1852	69.6	98
Cognitive	1	0	0.0	0
	2	5	0.5	11
	3	58	4.2	35
	4	281	20.2	74
	5	1041	75.1	98
Procedural	1	21	1.8	30
	2	11	0.9	17
	3	96	8.1	57
	4	301	25.5	94
	5	753	63.7	94

C)

	Sex	Number	Mean (SD)	Difference (95% CI)
Total	Male	1778	4.64 (0.67)	0.13 (0.07, 019)*
	Female	886	4.51 (0.77)	
Cognitive	Male	937	4.74 (0.52)	0.13 (0.06, 0.19)*
	Female	448	4.62 (0.63)	
Procedural	Male	841	4.53 (0.78)	0.12 (0.24, 0.22)*
	Female	438	4.41 (0.87)	

D)

	Academic vs Clinical	Number	Mean (SD)	Difference (95% CI)
Total	Academic	1488	4.51 (0.75)	0.20 (0.15, 0.25)*
	Clinical	1176	4.71 (0.62)	
Cognitive	Academic	912	4.62 (0.61)	0.18 (0.11, 0.24)*
	Clinical	473	4.82 (0.44)	
Procedural	Academic	576	4.31 (0.89)	0.33 (0.24, 0.42)*
	Clinical	703	4.64 (0.71)	

E)

	Subspecialty	Number	Mean (SD)	Difference (95% CI)	
Total	General	640	4.57 (0.70)	Vs. IBD: Vs. Hepatology: Vs. Therapeutics:	0.11 (0.00, 0.21)* -0.23 (-0.31, -0.14)* 0.10 (-0.09, 0.11)
	IBD	690	4.47 (0.78)	Vs. General: Vs. Hepatology: Vs. Therapeutics:	-0.11 (-0.21, 0.00)* -0.33 (-0.43, -0.24)* -0.10 (-0.20, 0.01)
	Hepatology	667	4.80 (0.52)	Vs. General: Vs. IBD: Vs. Therapeutics:	0.23 (0.14, 0.31)* 0.33 (0.24, 0.43)* 0.24 (0.12, 0.33)*
	Therapeutics	667	4.56 (0.74)	Vs. General: Vs. IBD: Vs. Hepatology:	-0.10 (-0.11, 0.09) 0.10 (-0.01, 0.20) -0.24 (-0.33, -0.12)*
Cognitive	General	303	4.62 (0.67)	Vs. IBD: Vs. Hepatology: Vs. Therapeutics:	-0.16 (-0.12, 0.09) -0.22 (-0.32, -0.11)* -0.09 (-0.21, 0.03)
	IBD	409	4.65 (0.58)	Vs. General: Vs. Hepatology: Vs. Therapeutics:	0.16 (-0.09, 0.12) -0.20 (-0.30, -0.10)* -0.74 (-0.19, 0.04)
	Hepatology	410	4.83 (0.44)	Vs. General: Vs. IBD: Vs. Therapeutics:	0.22 (0.11, 0.32)* 0.20 (0.10, 0.30)* 0.12 (0.01, 0.24)*
	Therapeutics	263	4.71 (0.55)	Vs. General: Vs. IBD: Vs. Hepatology:	0.09 (-0.03, 0.21) 0.74 (-0.04, 0.19) -0.12 (-0.24, -0.01)*
Procedural	General	337	4.53 (0.72)	Vs. IBD: Vs. Hepatology: Vs. Therapeutics:	0.31 (0.13, 0.49)* -0.23 (-0.36, -0.07)* 0.06 (-0.08, 0.21)
	IBD	281	4.22 (0.96)	Vs. General: Vs. Hepatology: Vs. Therapeutics:	- 0.31 (-0.49, -0.13)* -0.52 (-0.70, -0.34)* -0.25 (-0.43, -0.06)*
	Hepatology	257	4.75 (0.63)	Vs. General: Vs. IBD: Vs. Therapeutics:	0.23 (0.07, 0.36)* 0.52 (0.34, 0.70)* 0.28 (0.13 to 0.42)*
	Therapeutics	404	4.47 (0.83)	Vs. General: Vs. IBD: Vs. Hepatology:	0.06 (-0.08, 0.21) 0.25 (0.06, 0.43)* -0.28 (-0.42, 10.13)*

Patient directives to improve care for gestational diabetes: A systematic review of qualitative studies

Feng, Yuyang Julianne; Deng, Judy; Sivak, Allison; Yeung, Roseanne O; Nagpal, Taniya

Supervisor: Roseanne Yeung

INTRODUCTION

Gestational diabetes (GDM) increases the risk for maternal and fetal morbidity and patients have described unsatisfactory experiences with their prenatal GDM care. The objective of our systematic review was to synthesize directives for improving prenatal GDM care, as informed by lived experience of patients and their partners.

METHODS

This study is a systematic review of qualitative studies (PROSPERO CRD42023394014). Our search strategy was executed on January 21, 2023 in five databases (Medline, PsycInfo, CINAHL, Scopus, and Web of Science). No date restrictions were applied. Two independent authors used Covidence software to facilitate screening. After duplicate removal, a total of 4761 studies underwent screening and a total of 80 studies were included. Meta-aggregation followed by a thematic synthesis approach was used to analyze the qualitative data to identify patient-directives for GDM care. The Critical Appraisal Skills Programme qualitative checklist was used to assess quality and risk of bias.

RESULTS

Our search strategy was executed in six databases and a total of 80 studies were included. Directives for care include timely and comprehensive education around GDM and its management, active engagement of family members in care, personalized and patient-centered support and counseling, awareness and access to peer support, as well as sensitivity to and prevention of stigma associated with GDM.

CONCLUSIONS

Many patient and environmental factors affect the experience of GDM. Our systematic review findings identify several patient-reported directives for care, and our interpretation of additional directions through barriers and enablers experienced by patients. These findings provide rich direction for improving antenatal GDM care from the patient perspective.

Understanding Barriers to Referring Patients to a Deprescribing Clinic

Drs. Iffat Iqbal, Rahul Mehta, Pamela Mathura, and Winnie Sia

Supervisor: Winnie Sia

INTRODUCTION

Deprescribing is the process of discontinuing medications under medical supervision, that are no longer required or can cause more harm than benefit. A survey conducted at the Royal Alexandra Hospital (in 2022), more than half of the respondents (general internal medicine (GIM) physicians) indicated hospitalized patients would benefit from deprescribing. A deprescribing clinic staffed by GIM physicians and pharmacists was established and trialed for 6 months.

METHODS

Using the Model for Improvement with Plan-Do-Study-Act (PDSA) cycles, process mapping and multidisciplinary team meetings, a deprescribing clinic was initiated in July 2023. Patients from Royal Alexandra Hospital (GIM units), who met the deprescribing clinic criteria were triaged and referred. Two PDSA cycles were completed and evaluated to understand the barriers to clinic referral. A survey was developed and distributed to GIM physicians and pharmacists to assess their awareness of and barriers to referring patients to the deprescribing clinic. Data were analyzed using descriptive statistics.

RESULTS

For PDSA#1, in-person clinic appointments were offered to deprescribe proton pump inhibitor and 2 patients were referred and 1 seen. For PDSA#2 virtual appointments were offered and deprescribing medications expanded to all medications except opioids, antipsychotics, and benzodiazepines. One patient was referred but declined appointment. According to the initial physician and pharmacist survey results, the clinicians cited a lack of time to investigate medicines unrelated to the primary diagnosis (60%) as the primary reason for not referring, with 50% believing that primary care physicians should do the deprescribing.

CONCLUSIONS

Trial of a deprescribing clinic following hospitalization provided an opportunity to gain insight of polypharmacy, the roles of hospital and community-based physicians, the need for improved coordination between hospital and community physicians, and the role of community pharmacy in supporting deprescribing.

A quality assessment study to determine if tissue acquisition and specimen handling impact the diagnostic yield of endoscopic ultrasound-guided fine needle aspiration biopsy of solid mass lesions

S Khan, P Mathura1,, L Puttagunta, S Girgis, A Thiesen, J Zhang, J Nilsson, S Wasilenko, S Zepeda- Gomez, and G Sandha.

Supervisor: Gurpal Sandha

INTRODUCTION

Endoscopic ultrasound (EUS)-guided fine needle aspiration biopsy (FNAB) of solid mass lesions has a sensitivity and specificity between 50-100%. Tissue acquisition and specimen handling are factors that may contribute to this variability. At our institution, 3 endoscopists perform EUS. The aspirated material obtained is expressed onto slides for cytology (prepared by a nurse) and solid tissue fragments transferred into formalin. At the discretion of the endoscopist, aspirated material is collected in saline for cell block preparation. Our aim was to assess the impact of tissue collection and specimen handling on diagnostic yield of EUS-FNAB of solid mass lesions.

METHODS

A one year chart audit was completed for all patients undergoing EUS-FNAB of solid mass lesions.

RESULTS

A total of 184 patients underwent 200 EUS- FNABs. Pancreatic masses were the most common indication in 118/200 (59%) cases. A 22-gauge FNAB needle was used in 189/200 (95%) cases. A total of 285 needle passes were performed in 149 cases (mean 1.9/case). In the remaining 51 cases (26%), the number of needle passes was not specified. Tissue samples were transported in formalin in 190 cases, on cytology slides in 170 cases, and in saline for cell block preparation in 41 cases. Overall, a definite diagnosis was achieved in 149/200 cases (75%). Stratifying for needle passes, a definite diagnosis was achieved in 22/39 (56%), 71/85 (84%), 20/24 (83%), and 1/1 (100%) cases that had 1, 2, 3, and 4 needle passes. Of the 51 cases with unspecified needle passes, a definite diagnosis was achieved in 35 cases (69%). The diagnostic yield obtained with saline for cell block was similar to that obtained with formalin and cytology slides (30/41 [73%] vs. 144/190 [76%] and 132/170 [78%]).

CONCLUSIONS

For standard of care, increase the minimum number of needle passes, Document the number of needle passes in the endoscopy report and prepare Cytology slides and tissue in formalin.

Outcome of utilizing MELD 3.0 from a Canadian perspective: a retrospective study in a single tertiary-care transplant centre

Crystal Liu, Carlos Moctezuma Velazquez, Rahima Bhanji, Vincent Bain, Glenda Meeberg, Malcolm Wells

Supervisor: Malcolm Wells

INTRODUCTION

The model for end-stage liver disease (MELD) 3.0 has recently been implemented by UNOS in the United States to determine organ allocation priorities. It optimizes the existing MELD with added variables for sex and serum albumin. We conducted this study to assess whether utilizing MELD 3.0 would change classification or mortality outcomes in the Canadian context.

METHODS

The study was conducted at the University of Alberta Hospital. All patients registered for liver transplant between January 2015 through December 2023 were examined. The main outcome is survival up to 90 days from the time of waitlist registration. Each subject's baseline demographic was extracted, and their respective MELD, MELD-Na, and MELD 3.0 scores were calculated. Subjects were stratified by whether they were up or down-classified with the MELD 3.0 score, along with their respective mortality outcomes.

RESULTS

In total, 902 patients were listed for liver transplant between January 2015 through December 2023, and 512 subjects were enrolled in the study. The population studied had a median MELD 19.0 (15.0-26.0), MELD-Na of 21.0 (IQR 16.0-28.0), and a MELD 3.0 of 22.1 (IQR 16.9-28.6). The Harrell's C-statistics for MELD-Na and MELD 3.0 were 0.8739 and 0.8764, respectively. Overall, a net of 7.9% of subjects were correctly re-classified to a higher MELD 3.0 class, which would result in a meaningful increased likelihood of liver transplant for those subjects. This is similar to what was found based on the original MELD 3.0 model development by Kim et al with a net reclassification of 8.8%. We did not find a significant difference between male and female subjects who were re-classified, though the sample size was limited.

CONCLUSIONS

The MELD 3.0 score offers a more accurate mortality prediction than the MELD-Na score and should be more widely adopted in Canadian transplant centres.

N=512		MELD 3.0				
		6-9	10-19	20-29	30-39	>40
MELD-Na	6-9	16				
	10-19	4	166	25		
	20-29		8	171	14	
	30-39			5	72	8
	>40				2	21

N=89		MELD 3.0				
		6-9	10-19	20-29	30-39	>40
MELD-Na	6-9					
	10-19		13	4		
	20-29		2	35		
	30-39			1	18	6
	>40					10

89=100%		MELD 3.0				
		6-9	10-19	20-29	30-39	>40
MELD-Na	6-9					
	10-19		14.6%	4.5%		
	20-29		2.2%	39.3%		
	30-39			1.1%	20.2%	6.7%
	>40					11.2%

Overall

-Up-classified: 47 (20%)
-Down-classified: 19 (8%)
-Remain the same: 446 (72%)

Net Deaths

-Up-classified: 10
-Down-classified: 3
-Remain the same: 76
-Net gain: +7

% of Deaths

-Up-classified: 10
-Down-classified: 3
-Remain the same: 76
-Net gain: +7

Figure 1. Reclassification of liver transplant candidates between MELD-Na and MELD 3.0 from 2015-2023. (top) the number of patients, (middle) the number of deaths and (bottom) the proportion of death

Understanding Provincial Ambulatory Patient Concerns and Commendation Data

Jasmin Majumdar

Supervisor: Elaine Yacyshyn

INTRODUCTION

Patient feedback in the ambulatory care setting is an underutilized, valuable source of data. The purpose of this study was to gain a better understanding of physician actions and behaviors patients perceive positively and negatively.

METHODS

Using explanatory mixed methods, anonymous Alberta Health Services (AHS) ambulatory patient concerns and commendation data involving physicians across Alberta were retrieved and analyzed for 6-years (2017-2022). Quantitative phase/ analyses included: totals per health zone, facility, AHS concern and commendation categories. Qualitative phase/analyses included: a content analysis aligned to the Healthcare Complaints Analysis Tool (HCAT). Concern and commendations were mapped to the HCAT domains (clinical, relationship and management), themed and integrated into a joint display.

RESULTS

757 concerns and 166 commendation reports were reviewed from 53 and 29 ambulatory locations representing five healthzones in Alberta. After the COVID-19 pandemic, there was a 48% increase in commendations and a 23% decrease in concerns. The Edmonton healthzone received the most feedback. Concerns and commendations aligned to three AHS delivery of care categories: practice standards; care plan; diagnosis and assessment. Concerns also aligned to communication, and access to services AHS categories. Applying the HCAT, the majority (69%) of concerns were low severity, aligned to domains clinical and relationship,16 themes were developed. For commendations, the most common (77%) reason for providing a compliment was to acknowledge the action/behaviour, majority (72%) aligned to relationship, and 5 themes resulted. Data integration revealed a presence or absence of key actions and behaviors, including respecting patient time and dignity, providing patient-centered communication, and demonstrating professional competence. Patients want to be heard, treated kindly, cared for and respected.

CONCLUSIONS

Patients are more inclined to share concerns. Commendations and concerns refer to similar actions and behaviours from which improvement to the patient experience in ambulatory care settings can be made.

Optimizing Point-of-Care Glucose Chemstrip Utilization in Hospitalized Patients: A Quality Improvement Initiative

Kyle Moxham, Pamela Mathura, Darren Lau

Supervisor: Darren Lau

INTRODUCTION

Hospitalized adults commonly have routine point-of-care capillary blood glucose testing (CBG) ordered on admission. Excessive CBG can strain nursing resources without notable patient benefits. This study's objective was to reduce the frequency of unnecessary CBG in hospitalized General Internal Medicine (GIM) patients at the University of Alberta Hospital.

METHODS

Using the Model of Improvement with Plan-Do-Study-Act (PDSA) cycles, an evidence-based CBG rationalization algorithm was established and trialed (started in March 2024) using an educational approach targeting ordering physicians and nurses. A retrospective chart audit of 6 GIM units in September 2023 estimated baseline CBG utilization. To understand physician and nursing perspectives, a pre-intervention survey was developed and disseminated via paper and Google-Forms. The primary outcome measurement was the prevalence of patients with unnecessary CBG orders at the time of hospital discharge. Intervention impact was determined by chart audit. Descriptive statistics supported analysis.

RESULTS

A total of 321 charts were reviewed pre and post-intervention, with 84% (n = 270) of patients having CBG ordered on admission. The frequency of unnecessary CBG orders at discharge decreased 13.2% from 28.2% (48/170) to 15% (15/100). The average length of stay until CBG de-escalation improved from 10.6 days to 7.65 days (difference: -2.95 days). Patients who underwent CBG de-escalation at day 3 of admission (if eligible) improved 6.27% from 20.4% (11/54) to 26.67% (8/30) post-intervention.

CONCLUSIONS

CBG measurements in-hospital are frequently unnecessary resulting in inefficient use of nursing resources. The absence of established algorithms for reassessing POCT frequency may perpetuate unnecessary testing during hospitalization. Continued evaluation of this intervention is underway.

Authors:
Kyle Moxham, MD
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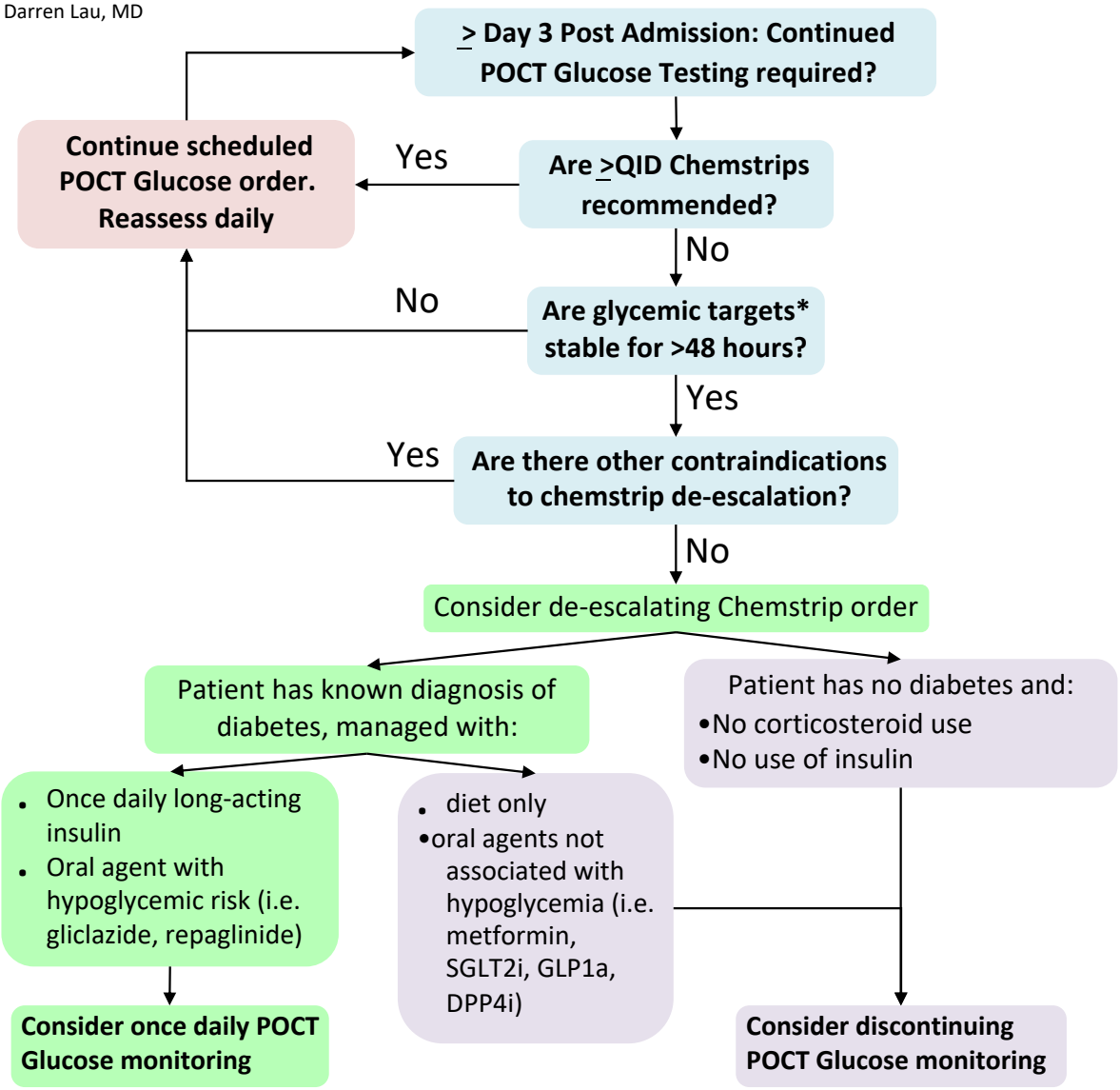
POCT Glucose Chemstrip Rationalization Algorithm



>QID Chemstrips Recommended:

- T1DM or T2DM on BBIT
- IV insulin infusion (ie DKA)
- HbA1c >8%
- Diabetes in Pregnancy
- DM patient NPO or on
- parenteral/enteral feed
  DM patient on corticosteroids

***AHS Policy for Glycemic Targets:**

- Non critically ill adult inpatient: 5-10 m m ol/L
- Critically ill patient: 6-10 mmol/L
  ACS patient: 7-10 mmol/L
- Frail, elderly or dementia: 5-12 mmol/L

Contraindications to de-escalation:

- Vital signs unstable
- NPO status
- Observation bed or ICU
- Active adjustments to insulin or
- PO agent dosing (within 48hr)
- <2 days from hypoglycemic episode (<4 mmol/L)
  <2 days from starting or dose adjustment to: systemic steroid, TPN/enteral nutrition, octreotide
- Receiving IV dextrose containing sol ut i on

A cronym s :

- DM: Diabetes mellitus
- POCT: Point of Care Test
- BBIT: Basal Bolus Insulin Therapy
- ACS: acute coronary syndrome

Algorithm adapted from Diabetes Canada Guidelines

What About Physician Wellness? Impact of a Quality Improvement Intervention

Isabella Pascheto, Pamela Mathura, Jennifer Ringrose, and Gillian Ramsay

Supervisor: Narmin Kassam

INTRODUCTION

Emergency department consultations with General Internal Medicine (GIM) physicians are required to ensure safe, effective care and to determine patient hospitalization. GIM physicians frequently care for patients in hospital wards while also completing an ED consultation request, resulting in delayed ED consultations, and difficulty balancing workload requirements of the ward and the ED, which may contribute to physician burnout. To streamline physician workload, a QI initiative, a GIM ED consultation service [with separate ward and ED clinical duties], was trialed. This study’s purpose was to evaluate the impact of this QI intervention on participating physicians' wellness.

METHODS

Using a pre-post design, two questionnaires adapted from the validated Mini-Z version 1.0 (Zero Burnout Program) work life measure for clinicians' survey were created and distributed via Google Forms to gather feedback from participating GIM physicians before and after the intervention. The data was analyzed using descriptive statistics and Mini-Z outcome measurement scales.

RESULTS

Thirteen physicians completed the surveys. Applying the Mini-Z scale, the GIM ED consultation service had no impact on well-being or burnout. A minor increase (2%) in satisfaction and decrease (1%) in stress level were identified, thus no change in the working environment occurred. Comparing question responses, job satisfaction improved (36%), job-related stress increased (24%), while “burnout” (23%) and “beginning to burn out” (9%) were both reduced.

CONCLUSIONS

Prioritizing wellness for physicians and all other healthcare providers should be considered when conducting QI initiatives. Consideration may improve intervention design, proactively incorporating wellness strategic actions, which may improve implementation success and sustainability.

A QUALITY ASSESSMENT OF THE ADEQUACY OF FLUID REPLACEMENT THERAPY FOR PATIENTS DIAGNOSED WITH ACUTE PANCREATITIS

Kinjal Patel, Maha Niazi, Samina Khan, Pamela Mathura, Julie Zhang, and Gurpal Sandha

Supervisor: Gurpal Sandha

INTRODUCTION

For acute pancreatitis (AP), aggressive fluid resuscitation therapy (FRT) is the cornerstone for initial management. However, results from the recent WATERFALL study show a higher incidence of fluid overload with aggressive FRT (bolus 20 ml/kg followed by infusion 3 ml/kg/hr of Ringer's lactate [RL]) compared with moderate FRT (infusion 1.5 ml/kg/hr RL after bolus of 10 ml/kg if hypovolemic). Given this evidence, we conducted a study to assess whether patients with AP received appropriate fluid therapy and monitoring at our institution.

METHODS

We completed a chart audit of all adult (≥ 18 years old) patients who presented to the ED from April 1, 2021 through March 31, 2022 and were diagnosed with AP. Patients were identified based on ICD-10 codes for a primary admission or discharge diagnosis of AP. Data variables collected included demographic information, cause of AP, comorbidities, laboratory tests, type and volume of fluids replaced, urine output, complications, and hospital length of stay (HLOS). Severity of AP was categorized as mild, moderate, or severe based on the revised Atlanta classification of AP. Descriptive statistics were completed.

RESULTS

A total of 250 patients (121 F, 129 M), mean age 53±19 years (range 19-96 years) were diagnosed with AP. Body weight was not available for 4 patients and thus excluded from this analysis. FRT variables stratified for the severity of AP are below:

CONCLUSIONS

Our quality assessment has identified a knowledge-to-practice gap in the use of FRT for patients with AP. To assist physicians in the decision-making process, we have developed an algorithm to improve FRT in AP. This will be implemented via an order set to standardize the amount of FRT and to improve monitoring of urine output. This algorithm will be tested using an improvement science approach in collaboration with healthcare professionals.

Table 1. Summary of results stratified by severity of pancreatitis.

	MILD AP	MODERATE AP	SEVERE AP	TOTAL
PATIENTS, n (%)	195 (80)	38 (15)	13 (5)	246
COMPLICATIONS, n (%)	15 (7)	4(11)	7(54)	26 (11)
DEATHS, n (%)	0(0)	0(0)	2(15)	2(1)
AVERAGE HLOS, days	5	7	28 88	-
Average MAP, mm Hg	100	98	0/13 (0)	99
PMHx of heart failure, n (%)	8/195 (4.1)	0/38 (0)		8/246 (3.3)
FLUID BOLUS **RECEIVED, n (%)** **VOLUME, ml/kg mean±SD**	 149 (76) 15±2	 33 (87) 17±5	 11 (85) 22±5	 193 (78) 16±2
MAINTENANCE FRT, n (%) **<1.5ml/kg/hr** **1.5-3ml/kg/hr** **>3 ml/kg/hr**	 90 (46) 102 (52) 3(2)	 12 (32) 26 (68) 0(0)	 3 (23) 7 (54) 3(23)	 105 (43) 135 (55) 6(2)
URINE OUTPUT **RECORDED, n (%)** **VOLUME, ml/24 hrs mean±SD**	 13 (7) 435±221	 1 (3) 30	 5 (39) 939±639	 19/246 (7) 546±244

Advanced Hepatic Echinococcosis: A Case Report

Sophia Quan, Malcolm Wells

Supervisor: Malcolm Wells

INTRODUCTION

Alveolar echinococcosis (AE) is a rare and potentially fatal disease caused by the parasite echinococcus multilocularis (EM). Humans become infected through contact with definitive hosts and ingestion of contaminated food and water. The liver is primarily affected but there is potential for metastatic spread. AE has a clinical latency time of 5-15 years and often resembles a malignancy in appearance and growth.

METHODS

Case report.

RESULTS

A 49-year-old farmer was admitted to a Saskatchewan hospital for a 2-week history of abdominal pain, jaundice, and weight loss. Computed tomography of the abdomen and pelvis showed a necrotic mass in the gallbladder fossa with involvement of the biliary tree and spleen. This was thought to be metastatic cholangiocarcinoma until the gallbladder biopsy returned as echinococcus, confirmed with serology and a nucleic acid test. The patient was then diagnosed with advanced hepatic AE with metastasis to the gallbladder, biliary tree, and spleen. While invasive surgery is curative, the patient's disease was too extensive for resection. He was started on albendazole and reviewed by our team for a liver transplant assessment 10 months later. There is limited literature on liver transplantation in advanced AE as it may not be curative. Immunosuppression may also expedite residual parasite growth leading to aggressive disease recurrence. The patient developed a hepatocutaneous (HC) fistula, and complete parasite removal would have require a liver transplant, splenectomy and HC fistula excision. Given his stability on albendazole, the surgical complexity and possibility of aggressive disease recurrence post-transplant, the multidisciplinary committee decided against liver transplantation. He continues to do well on albendazole 15 months after initial presentation.

CONCLUSIONS

This case highlights the complexities in management of advanced hepatic AE. Although not curative, benzimidazole is effective in slowing disease progression in unresectable cases. Further studies are needed to assess the role of liver transplant in advanced hepatic AE.

Active Mind, Active Body in Action: Assessing the Impact of Medical Student Volunteerism in the Hospital

Jaslyn Rasmuson, Kareena Nanda, Julian Lau, Pamela Mathura, and Winnie Sia

Supervisor: Winnie Sia

INTRODUCTION

Active Mind, Active Body (AMAB) is a novel medical student-led initiative, started in July 2021 at the Royal Alexandra Hospital. AMAB aims to reduce the mental and physical isolation of hospitalized patients through social and physical activities. It exposes pre-clinical undergraduate medical students (UMS) to medicine specialties and promotes an interdisciplinary approach to integrating social determinants of health into patient care. This study's purpose was to evaluate the program and assess the impact on participating UMS.

METHODS

Using a convergent mixed method approach, data was collected from the following sources: anonymized patient interaction records quantifying the volume of participating patients and type of interactions, a post-shift volunteer feedback form, and a program evaluation survey that was created and distributed via Google Forms to gather participating students' perspectives and experiences. Data was analyzed using descriptive statistics and thematic analysis.

RESULTS

424 encounters with 220 patients were completed from July 2021 to August 2023. About half of the interactions (49%) were longer than 30-minutes. Nearly all (98%) of patients had visits that included socialization, and some included cognitive activities (27%) and/or physical activity (22%). Thirty-four volunteers (56%, 34/61) completed the survey, revealing that most UMS perceived AMAB as valuable for patients (94%) and meaningful for volunteers (88%). UMS (67%) reported that AMAB provided exposure to different medical specialties, and most (74%) felt their involvement would improve their approach and interactions with patients. UMS noticed an improvement in communication skills, interprofessional collaboration, and patient-physician relationship building. Opportunities for program improvement included diversifying activities and implementing UMS peer-to-peer mentoring.

CONCLUSIONS

The AMAB program improved the hospital experience for patients while providing early impactful clinical education for medical students. These findings offer a replicable model adaptable to various medical education programs.

Prescribing Improvement for the Prescription Refill Process

Kayla Sage, Phillip Deluca, Wendy Johnston, Sheri Koshman, Kimberly Neigel, Jacques Romney, Jeremy Theal, Pamela Mathura, Elaine Yacyshyn

Supervisor: Elaine Yacyshyn

INTRODUCTION

Managing prescription refills in ambulatory care can be complex and time-consuming. This process was highly variable and inefficient due to paper-based workflows, requiring extensive communication between physicians, medical office assistants (MOA) and community pharmacies. The purpose of this study was to determine the impact of the Connect Care electronic medical record (CC-EMR) workflow for the physician prescription refill process in the ambulatory care setting.

METHODS

Using a pre-post research design guided by the Model of Improvement with Plan-Do-Study-Act (PDSA) cycles. Two PDSA cycles were completed and evaluated. Interventions included direct electronic faxing of prescriptions in CC, educational tools, 1:1 training and communication strategies. Pre-and post-intervention surveys were developed and disseminated to physicians and MOAs, descriptive statistics were completed.

RESULTS

Physician pre (N=100) and post-intervention (N=84) and MOA pre (N=63) and post-intervention (N=32) surveys were completed. Physicians reported an overall decrease in time spent completing prescription refills, with a 23.3% increase in spending ≤30 minutes/week, 12.5% decrease in 2 hours/week, and a 1.9% decrease in 3+ hours/week. Physician satisfaction improved by 59.3%, while dissatisfaction decreased by 40.0%. Physicians and MOAs perceived numerous benefits, including a reduced need for a printer to sign prescriptions (77.0%), lowered risk of delayed prescriptions (62.2%), reduced telephone calls to pharmacies (58.1%), ability to immediately refill prescriptions from any location and at any time (52.7%), and reduced need to physically come into work to complete this task (51.4%).

CONCLUSIONS

Understanding physician and MOA perspectives and challenges in a prescription refill process led to a CC-EMR workflow standardization. Streamlining this process improved satisfaction among physicians and MOAs while reducing workload, inefficiencies, and the risk of errors. This workflow innovation has led to inpatient and provincial use, which spread beyond the initial scope of the study, indicating the benefit of this project on provider usage.

Virtual Kidney Care during the COVID-19 Pandemic

Yilun Wu, Epsita Shome, Bhavneet Kahlon, Jennifer MacRae, Chandra Thomas, Nathan Gallagher, Elena Qirjazi.

Supervisor: Elena Qirjazi

INTRODUCTION

The COVID-19 pandemic necessitated shifting clinical encounters to virtual care whenever feasible, including at the Alberta Kidney Care South (AKC-S) Kidney Care Clinics (KCC). KCC provides multidisciplinary care for patients with advanced (Stage 4-5) chronic kidney disease (CKD) in Southern Alberta. We studied the implementation of virtual care in our clinics and its effect on clinical and biochemical patient outcomes.

METHODS

We retrospectively compared information extracted from local database in two time periods: 1) pre-pandemic control period: March 1, 2019-February 29, 2020; and 2) pandemic period: July 15, 2020-July 14, 2021 (with brief washout period). The uptake outcome was the proportion of virtual patient encounters. Patient clinical outcomes included mortality, dialysis starts, dialysis modality and dialysis start setting, hospitalization, and emergency visits. Biochemical outcomes include proportion of patients achieving CKD bloodwork targets.

RESULTS

During the two periods, the number of patients, clinic visits, and patient demographics were similar. In the control period, 97.83% of the appointments were in-person, compared to 33.36% in the pandemic period (p-value<0.0001). In this latter period, out of the virtual visits, 87% were by phone and 13% via Zoom. Patient clinical outcomes were similar between the two periods, except there were increased peritoneal dialysis starts and fewer hospitalization days and emergency visits during the pandemic period. Biochemical outcomes showed mixed results with slightly lower rates of achieving targets for hemoglobin and calcium and higher rates for other phosphate and parathyroid hormone in the pandemic period.

CONCLUSIONS

During the pandemic, there was a significant uptake of virtual care with no significant negative effects on patient outcomes. Further pragmatic studies are needed to establish the safety of virtual care and both patients’ and providers’ perspectives.