Queen's University

45th Annual Anesthesiology Research Day

Friday April 26, 2024
Donald Gordon Centre
Kingston, Ontario

Supported by the Galway Visiting Lectureship

Queen's University
45th Annual Anesthesiology Research Day

Scientific Program Director and Residency Research Coordinator:
Ian Gilron, MD, MSc, FRCPC

Research Day Co-moderators:
Glenio Mizubuti, MD, MSc **Rachel Rooney,** MD, FRCPC

Queen's University Judges:
Lindsey Patterson, MD, FRCPC **Anthony Ho**, MD, MSc, FRCPC

The Galway Visiting Lecturer: **Harsha Shanthanna,** MD, PhD, FRCPC

Department Head:
Ramiro Arellano, MD, MSc, FRCPC

Research Committee Chair:
Ian Gilron, MD, MSc, FRCPC

Research Day Administrator:
Charlotte Hannah

Clinical Research Director:
Tarit Saha, MD, MSc, FRCPC

Research Facilitator:
Rachel Phelan, MSc

Research Coordinator:
Debbie DuMerton, RN, CCRP

Research Coordinator:
Hala Elkerdawy, MD

Research Coordinator:
Grace Pavlatos-Jones, RN, CCRP

Research Coordinator:
Aftab Malik, MSc

Research Coordinator:
Reegan Tod, BSc

Institutional support:
• Queen's University • Kingston Health Sciences Centre (KGH & HDH Sites) • Providence Care

Held on April 26, 2024 – Donald Gordon Centre, Kingston, Ontario, Canada.

Funded by Educational Support from:

The Galway Visiting
Lectureship

SCIENTIFIC PROGRAM OUTLINE

0800 – 0805 **Opening Remarks**

– Dr. Ramiro Arellano

0805 – 0815 **Research Day Introduction**

– Dr. Ian Gilron

Oral presentations – order of presentations to be announced

0815 – 0945 **Oral presentations (6)**

0945 – 1015 **Wellness break**

1015 – 1145 **Oral presentations (6)**

1145 – 1245 **Lunch on site**

1245 – 1400 **Oral presentations (5)**

1400 – 1430 **Wellness break**

EACH 10-MINUTE ORAL PRESENTATION WILL BE FOLLOWED BY A 5-MINUTE QUESTION PERIOD

The Queen's Judges will be:

***Dr. Lindsey Patterson*,** Queen's Dept of Anesthesiology & Perioperative Medicine

***Dr. Anthony Ho*,** Queen's Dept of Anesthesiology & Perioperative Medicine

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1430 – 1530 ***Dr. Harsha Shanthanna*,** Professor, Department of Anesthesia, McMaster University

* Guest Lecture *

"Perioperative pain management: theory, decision making, and practice"

Wine & Cheese to follow with * Awards Presentation * (Donald Gordon Center)

<u>Oral Presentations</u> (alphabetical order)

Saam AZARGIVE, PGY-3
A Systematic Review of Indications, Techniques, and Outcomes in Endotracheal Extubation of the Anesthetized Adult Surgical Patient (proposal)

Danielle BOURGEOIS-LAPICCIRELLA, PGY-1
Investigating the usage and reducing wastage of nitrous oxide at KGH: a quality improvement initiative (proposal)

Milena BULLEN, PGY-1
The Development and Implementation of a Knowledge Translation Fellowship Program in Anesthesiology and Pain Management for Low- and Middle-Income Countries (proposal)

Toros CANTURK, PGY-1
Adductor Canal Block Quality Improvement Project (proposal)

Stephanie CHEVRIER, PGY-2
Development, Implementation and Assessment of a Real-Time Remote Method for Operationalizing Regional Anesthesia Procedural Techniques: Systematic Review Update (proposal)

Jared COHEN, PGY-4
A Novel Treatment Approach to Complex Regional Pain Syndrome (CRPS): A Feasibility Study of Combined Peripheral Nerve Block and Physiotherapy (update)

Taryn DAVIDSON, PGY-3
Perioperative Stroke in a Patient Undergoing Major Thoracic Surgery: A Case Report (case report)

Derek DIONNE, PGY-3
Feasibility trial of remotely delivered prehabilitation program in colorectal cancer patients: protocol paper (proposal)

Hailey GOWDY, BSc, PhD candidate (Queen's University DBMS)
An epidemiological study of the circadian control of biopsychosocial outcomes in chronic pain (update)

Noah LETOFSKY, PGY-2
What complications relevant to airway management have been reported in patients with achalasia in the literature? (update)

Matthew MACHINA, PGY-3
Endotracheal tube anatomy and endobronchial intubation - is the Parker tube different? (proposal)

Kristina NAZZICONE, MSc, BMSc (Queen's University School of Medicine)
Genicular Embolization vs. Neurolysis Intervention for knee osteoarthritis: protocol for the GENI Knee OA study (proposal)

Ciara O'CONNOR, MSc candidate (Queen's DBMS)
Microglial activation is regulated by circadian rhythms in chronic neuropathic pain (update)

Taylor PERRY, PGY-1
Cardiac changes after low dose carbetocin for elective Cesarian section (proposal)

Michael TAYLOR, PGY-2
Real-Time Remote Supervision and Teaching for Regional Anesthesia (Update)

Kendall VERHULST, PGY-2
A Scoping Review of IV Dexmedetomidine in Obstetrical Anesthesia (update)

Amanda ZACHARIAS, MBI, PhD candidate (Queen's DBMS)
Circadian regulation of genes and networks are associated with chronic low back pain (update)

Poster Presentations

Doriana Taccardi	**The CircaMS Study: Circadian rhythmicity as a biomarker for symptomatic phenotypes in MS**
Vina Li	**Circadian rhythmicity of neuropathic pain in a mouse model of Multiple Sclerosis**
Natalie Wilcox	**Tracking immune cells in vivo: use of a photoconvertible mouse to identify tissue-origin for cell migration in spinal cord injury**
Julia Liu/Nader Ghasemlou	**The effect of Lyme disease Borrelia burgdorferi on the activation of sensory neurons**

A Systematic Review of Indications, Techniques, and Outcomes in Endotracheal Extubation of the Anesthetized Adult Surgical Patient

Azargive, Saam[1]; Jakubowski, Josephine[1]; Mizubuti, Glenio[1]; Ho, Anthony[1]; Cupido, Tracy[1]; Pullattayil, Abdul[3]; Cohen, Natasha[2]; Leitch, Jordan[1] (Supervisor).

[1]Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Canada; [2]Department of Otolaryngology – Head & Neck Surgery, Queen's University, Kingston, Canada. [3]Department of Library Services, Queen's University, Kingston, Canada

BACKGROUND: The removal of an endotracheal tube in an anesthetized patient, also known as deep extubation, is a commonly used technique with limited description in the literature. While some evidence exists on the risks and complications of the technique, material on how to safely execute this technique remains obscured.

PURPOSE: The purpose of the proposed study is to characterize the factors in the decision-making for performing deep extubation. This includes indications, contraindications, anticipated complications, and described techniques and anesthetic agents. The results of this study will inform the development of a survey of a larger body of anesthesiologists in order to construct a means for educators to explore the topic. A protocol with relevant evidence, teaching strategies, and a unified conceptualization of the technique for extubating anesthetized patients will be developed.

METHODS: A literature search was performed on June 3-23, 2022 (J.J and A.P.). The search strategies were not limited to any study types. We supplemented the search with book chapters, theses/dissertations, and editorial or narrative reviews to include any other forms of description and evidence surrounding the topic of deep extubation. Inclusion criteria involved studies with human surgical patients, adults >18 years of age, intubation of an endotracheal tube, and extubation occurring while not awake. Exclusion criteria included pediatric airways, regional anesthesia techniques, non-human or animal studies, non-English studies, and papers unable to be accessed through university library and online databases. Data collection focused on design, sample size, population, indications and contraindications followed by authors, description of techniques and procedural skills used, and medications as well as any documented outcomes and complications.

PROGRESS: In total, 2,761 articles were identified from the initial 3,243 after the removal of 482 duplicates. Two independent investigators (S.A. and J.J.) screened the final search results using study titles and abstracts for possible inclusion. When possible, the full report was screened before inclusion and authors were contacted whenever full reports were not available. Disagreements were settled with the principle investigators (J.L. and N.C.) and a kappa agreement score was calculated. The initial analysis included exploration of the use of laryngeal mask airways, however this was later rescinded to only include studies using laryngeal mask airways as exchange or transition airways (i.e. Bailey maneuver). Our search yielded 34 papers which were assessed for full eligibility. After subsequent screening to remove previously unidentified duplicates and studies that violated inclusion criteria, 17 papers were identified for final inclusion, 8 RCTs, 1 observational study, and 8 case reports.

Investigating the usage and reducing wastage of nitrous oxide at Kingston General Hospital: a quality improvement initiative

Danielle Bourgeois-Lapiccirella, Dr. Christopher Haley and Dr. Jessica Burjorjee

BACKGROUND:

Nitrous oxide (N2O), while being a useful clinical tool, has a significant impact on our environment. Its atmospheric life is approximately 120 years, with a global warming potential of 265[1]. Hospitals that have previously investigated their piped nitrous oxide systems have determined that a significant proportion of nitrous oxide is wasted, while only a small amount is used clinically. The source of waste can be leaks within the piped system, over-ordering, stock expiration, and theft, among others[2,3]. At Kingston General Hospital (KGH), we have a 12-tank supply of nitrous oxide, with each tank holding 15000 litres of N2O. In addition, we have 14 "backup" tanks of N2O available. Based on suspected low clinical use of N2O, coupled with a large stock and an old pipeline, we feel that this QI project could lead to reducing our emissions, cost savings, and decreased occupational exposures to N2O.

OBJECTIVES:

The objectives of the project will be to
(1) determine the amount of nitrous oxide that is ordered each month at KGH,
(2) determine monthly clinical usage of nitrous oxide at KGH, and
(3) identify the presence or absence of nitrous oxide wastage, and, should there be wastage, identify the source.

To determine the amount of nitrous oxide that is ordered at KGH, we will collaborate with important stakeholders, including the purchasing department, maintenance, and equipment team to obtain access to the tank logbooks, manifold and pipeline maintenance schedules, and purchasing agreements/receipts.
To determine monthly clinical usage of nitrous oxide at KGH, we will be collecting both qualitative data through an informal survey and quantitative data through our anesthetic machines.
After identifying the sources of nitrous oxide wastage, we plan to further collaborate with important stakeholders to implement waste reduction strategies, which could include decommissioning our main nitrous oxide manifold and replacing this with portable cylinders at the back of our anesthetic machines.
Once a reasonable change has been implemented, we will proceed to re-collect the data and reassess nitrous oxide procurement vs clinical usage. Our primary metric for this project is to attain a goal of zero nitrous oxide wastage at KGH, while our secondary metric is cost savings.

REFERENCES:

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2. YouTube. (2021, January 27). *Nitrous Oxide Mitigation: Launching the UK and Roi National Audit.* YouTube. https://www.youtube.com/watch?v=OreKYfF0d8s
3. Centre for Sustainable Healthcare. *The Nitrous Oxide Project*. (2022, April 21). Accessed March 2024. https://sustainablehealthcare.org.uk/what-we-do/sustainable-specialties/anaesthetics/nitrous-oxide-project

The Development and Implementation of a Knowledge Translation Fellowship Program in Anesthesiology and Pain Management for Low- and Middle-Income Countries

Presenter: Dr. Milena Bullen **Supervisors:** Dr. Joel Parlow and Dr. Gregory Klar
Collaborators: Dr. Ana Johnson, Dr. Gaston Nyirigira, Dr. Paulin Banguti, Dr. Francoise Nizeyimana, Dr. Dylan Bould, Dr. Jon Bailey, Dr. Christopher Haley

Partnerships: Queen's University Departments of Anesthesiology and Perioperative Medicine and Public Health Sciences, the University of Rwanda Department of Anesthesiology and Critical Care, the Canadian Anesthesiologists' Society International Education Foundation, University of Ottawa Department of Anesthesiology and Pain Medicine, Dalhousie University Department of Anesthesia, Pain Management & Perioperative Medicine, and the Royal College of Physicians and Surgeons of Canada.

Funding: This fellowship received three years of funding from an International Development, Aid and Collaboration (IDAC) grant provided by the Royal College Canada International (RCCI).

Aim: The Knowledge Translation Fellowship Program aims to enhance the clinical application of current evidence in Rwandan perioperative care, through postgraduate medical education and faculty development.

Methods: An admissions process is completed to select two practicing anesthesiologists as fellows per year. Each fellow is assigned one Rwandan and one Canadian anesthesiologist mentor whose training background and research interest align with the fellow's chosen field of interest. The fellowship consists of a two-month didactic training component, where the fellows travel to Canada to learn the foundations of knowledge translation, quality improvement, and quantitative and qualitative research methods through training in the clinical environment, lectures, interactive workshops, seminars, and online modules. While in Canada, fellows collaborate with their mentors to outline a proposal for a knowledge translation/quality improvement project. Fellows then return to Rwanda to implement these projects on a part-time basis back at their home institution. Fellows who have completed the program are encouraged to mentor incoming cohorts of fellows to help support the sustainability of the program.

Preliminary Results: Over the course of three years, six fellows will graduate from the program; to date, four fellows have developed KT projects. During the first year of the program, a regional anesthesia block room was created to enable the provision of pre-operative regional anesthesia at the Kigali University Teaching Hospital. Concurrently, an analysis was completed to determine opportunities and barriers for the sustainability of a local cardiac surgery program in Rwanda. The projects developed by the second cohort of fellows include the development of a pediatric anesthesia fellowship program in Rwanda, and a study to evaluate and enhance awareness of the diagnosis and management of chronic pain in rural hospitals in Rwanda. The third cohort of two fellows has been admitted to the program and will begin in September 2024.

Next Steps: Plan to implement a formal evaluation process to gather feedback from fellows throughout and at the end of each year to help improve the quality of the fellowship experience. This will be guided by the theory of change approach informed by Guskey's five-level framework [1]. Plan to develop online modules for the residency curriculum at the University of Rwanda and have the graduated fellows mentor residents in quality improvement and knowledge translation methods.

Conclusion: Providing knowledge translation training and mentorship to physicians can lead to sustainable changes in clinical care, allowing physicians to critically evaluate their current practices, identify local needs and barriers to care, and develop and implement responses to the identified problems. The goals of this approach are to develop and improve evidence-based clinical practices, promote retention of trainees in Rwanda and empower individuals to become local champions of change. This fellowship provides the tools for physicians in LMICs to develop and continuously evaluate and improve their impactful work for years to come.

References:

1. Guskey T. Does it make a difference? Evaluating professional development. 2011. *Journal of Educational Leadership.* 59:45-51.

Adductor Canal Block (ACB) Quality Improvement Project

Dr. Toros Canturk (MD, PGY1)
Principal Investigator: Dr. Tracy Cupido

Background: The complication rate after ACB is difficult to ascertain because of its rare occurance[1] . One of the largest studies in this area was performed by Beckman et al[2], who investigated 28,196 knee surgeries. They found only 18 cases (0.06%) of saphenous nerve injury and only 5/18 was attributed to the ACB (0.018%). Last fall, we were informed by our orthopedic surgery colleagues that they were observing more than usual nerve-injury rates after ACBs. We decided to propose a study to assess the patients that were experiencing query nerve injury to better understand their etiology and guide management. We investigated the incidence of neuropraxia after ACBs in our centre. Also, establish a pathway for improved follow-up of ACBs.

Study Purpose: Our 4 purposes with this study as follows:

1) Audit incidence of neuropraxia after adductor canal in our centre.
2) Compare our incidence rate to the literature.
3) QI- review techniques for performing adductor canal.
4) Develop a follow-up algorithm for potential neuropraxia of any etiology post-operatively.

Research Question: In keeping with our purposes above, our research questions are 1) Does our incidence rate of nerve injury after ACBs comparible to the literature? 2) Are there any alterations based in the literature that we can do in our technique, medications, volume and other factors to optimize our ACBs and 3) Once we finalize the development of our neuropraxia algorithm, how can we incorporate it into currently utilized post-operative follow-up programs?

Design and Methods: This is a single centre quality improvement study from Kingston Healthsciences Centre. Patients who were reportedly experiencing nerve injury were called by phone and ones that continued to have problems were brought into the clinic for further examination and management. The literature search, auditing our current practices, development and implementation of the nerve injury screening pathway is currently underway.

Next Steps: The literature search to optimize our ACBs is currently underway. The audit on current practice on the patients that were seen in the clinic is completed and findings were presented in the Acute Pain Management Service meeting early March. We will compare-and-contrast the "best practices" into our current practices and results will be shared in our Acute Pain Management Service meeting for the consideration of rest of the faculty in the incoming months. Recognizing the crucial importance of early detection of nerve injuries caused by nerve blocks, surgeries or other etiologies in the post-operative period, we will develop and implement a nerve injury pathway for patients undergoing surgery and having adductor canal block both before and after the surgery. Furthermore, find a feasible and cost-effective way to incorporate this pathway into the post-operative journey of the patient.

References:

1) **https://pubmed.ncbi.nlm.nih.gov/23074997/**

2) **https://journals.sagepub.com/doi/abs/10.1177/15563316231194614**

Remote Learning and Supervision of Ultrasound-Guided Nerve Blocks

Glenio Mizubuti, Stephanie Chevrier, Omar Elmoursi

Background: Ultrasound-guided regional analgesia techniques have become increasingly popular. They can reduce and at times eliminate the need for opiate analgesics, thereby improving patient safety, reducing length of hospital stay and associated medical costs, and increasing patient satisfaction. However, a major barrier to the mainstream uptake of such regional anesthesia techniques pertains to training physicians; these techniques require acquisition of new skills under expert guidance, which is often challenging given the daily time-sensitive and competing demands placed upon anesthesiologists. With further staff shortages and increasing demands brought on by the COVID-19 pandemic, expert availability for one-on-one guidance has become even more limited. As a result, many opportunities for providing regional analgesia to patients who would likely benefit from it may be missed, and nerve blocks may be performed in the absence of expert guidance.

Study Purpose: Performing a review of the current literature on remote learning and supervision of ultrasound-guided nerve blocks to gain insight on the feasibility of this method as a tool for real-time remote teaching and learning of standard-of-care nerve blocks.

Research Question: Is remote learning and supervision of ultrasound-guided nerve blocks an effective training method for teaching in medicine (students, residents, continuing education, etc.)?

Design and Methods: This study consists of a systematic review. In collaboration with a Health Sciences Librarian, an initial search strategy in the Embase, Web of Science, Medline and Cochrane databases yielded approximately 1500 results. These articles' titles and abstracts were screened with pre-established inclusion and exclusion criteria. Included articles focused on medical students, residents, fellows or practicing physicians who received training in ultrasound-guided nerve blocks remotely. The intervention of interest was synchronous remote learning and supervision methods for ultrasound-guided nerve block training (e.g. web-based platforms, virtual reality simulations, teleconferencing). The initial screening yielded 29 results, for which full-text reviews will be undertaken to extract important themes such as knowledge acquisition, technical skills, procedural competency, patient safety, rate of complications and learner satisfaction relating to the effectiveness of remote learning and supervision methods.

References:

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3. Burckett-St.Laurent, D.A. et al. (2016) "Teaching ultrasound-guided regional anesthesia remotely: A feasibility study," Acta Anaesthesiologica Scandinavica, 60(7), pp. 995–1002. Available at: https://doi.org/10.1111/aas.12695.
4. Fang, S. et al. (2022) "Application of distant live broadcast in clinical anesthesiology teaching," American journal of translational research, 14(3), 2073–2080.
5. Miyashita, T. et al. (2013) "FaceTime® for teaching ultrasound-guided anesthetic procedures in remote place," Journal of Clinical Monitoring and Computing, 28(2), pp. 211–215. Available at: https://doi.org/10.1007/s10877-013-9514-x.
6. Moore, D.L., Ding, L. and Sadhasivam, S. (2012) "Novel real-time feedback and integrated simulation model for teaching and evaluating ultrasound-guided regional anesthesia skills in pediatric anesthesia trainees," Pediatric Anesthesia, 22(9), pp. 847–853. Available at: https://doi.org/10.1111/j.1460-9592.2012.03888.x.

A Novel Treatment Approach to Complex Regional Pain Syndrome (CRPS): A Feasibility Study of Combined Peripheral Nerve Block and Physiotherapy - Update on a Research Protocol

Dr. Jared Cohen
Supervisor: Dr. Tracy Cupido

Complex regional pain syndrome (CRPS) is a chronic, and often debilitating, pain condition. Development of CRPS is commonly associated with local trauma, such as a fracture, sprain, or surgery. However, many patients with CRPS will report only very trivial injuries to the area, or no injury at all. Patients with CRPS can develop a number of signs and symptoms of the condition, including hyperalgesia and allodynia, temperature changes in the limb, motor dysfunction, and limb edema[1]. The pathophysiology of CRPS is poorly understood. Some evidence has suggested that microvascular dysfunction and peripheral ischemia may play a key role in CRPS development[2].

The successful use of peripheral nerve blocks for CRPS has been reported in the literature[3]. Though the mechanism is not fully defined, vasodilation after a peripheral nerve block may improve microvascular dysfunction in the limb, and the analgesic effects may allow patients to more actively participate in physiotherapy. Unfortunately, there is very little quality evidence investigating the use of peripheral nerve blocks in CRPS.

We intend to assess the efficacy of a single-shot axillary brachial plexus block plus physiotherapy as a novel treatment protocol for CRPS. Our primary hypothesis is that providing a brachial plexus block in conjunction with a physiotherapy program would be superior to physiotherapy alone in treating pain and function in CRPS. Since this is a novel treatment protocol for CRPS, the purpose of our proposed study is to determine the feasibility of conducting a fully powered clinical trial.

Participants who meet Budapest criteria for CRPS will be randomized to either receive a single-shot axillary brachial plexus nerve block followed by an examination and manipulation of the limb by a physiotherapist, or receive no regional anesthesia. All participants will then complete a regimen of six weekly physiotherapy sessions, with an at-home graded motor imagery program.

The primary outcome of this feasibility study will be the ability to recruit 60 patients (30 per arm) for study participation within 2 years. Attrition, data completeness, therapeutic compliance, study cost, and time spent on the study by staff will be assessed as secondary feasibility outcomes. Data for the proposed trial primary outcome of limb range of motion and secondary outcomes of CRPS Severity Scale and Patient Global Impression of Change scales, will also be assessed at baseline, and after two, four, and six weeks of physiotherapy.

1. Shim, H., Rose, J., Halle, S. & Shekane, P. Complex regional pain syndrome: a narrative review for the practising clinician. *Br. J. Anaesth.* **123**, e424–e433 (2019).
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Perioperative Stroke in a Patient Undergoing Major Thoracic Surgery: A Case Report

AUTHORS: Davidson, Taryn[1]; Edgeworth, David[1]; Shatenko, Sergiy[1]; Leitch, Jordan (Supervisor)[1]
AFFILIATIONS: [1]Anesthesiology and perioperative Medicine, Queen's University, Kingston, Canada

Purpose: Perioperative stroke is defined as a brain infarction of ischemic or hemorrhagic etiology that occurs during surgery or within 30 days after surgery[1]. Perioperative stroke can be a devastating complication after surgery, with a rate of disability and mortality that is higher than stroke unrelated to surgery[2]. Perioperative stroke is relatively underrecognized and uncharacterised compared to other complications in the perioperative period[3], and many physicians and patients underestimate the risk of perioperative stroke[4]. In fact, the risk of a clinically silent stroke may reach 7% in patients 65 years and older undergoing noncardiac surgery[5]. Low rates of recognition or delayed recognition in the perioperative period may be partly explained by low awareness of this complication or lack of validated screening tools that are capable of capturing the diverse and sometimes subtle manifestations of perioperative stroke[3]. In this case report, we discuss our experience with the diagnosis of a perioperative stroke. We hope to contribute to the literature aimed at characterizing the diverse presentation of this complication in the perioperative period.

Clinical Features: A 71 year old female with hypertension, chronic obstructive pulmonary disease (COPD), non-insulin dependent diabetes, smoking history and prior stroke (no residual deficits) presented for an extensive resection of locally-advanced pleomorphic lung adenocarcinoma on October 6th, 2023. The resection involved a right-sided thoracotomy, right lower lobe resection, right middle lobe wedge resection, right upper lobe posterior segmentectomy, and chest wall resection. Postoperatively, she was transferred from PACU to a high-dependency unit for ongoing management. She was stable overnight with unchanged oxygen requirements. On postoperative day (POD) 1, she was assessed by the acute pain service and was noted to be quite confused, oriented to person only. Further questioning also revealed new vision changes. On physical exam, she had a temporal visual field defect of the right eye and nasal visual field defect of the left eye, concerning for right homonymous hemianopsia. There were no other apparent cranial nerve or focal deficits, with a NIHSS score of 3. An urgent stroke consult was called and she immediately underwent a CT head that established a left occipital ischemic infarct (early subacute moderate-to-large ischemic event in the left posterior cerebral artery distribution) causing moderate mass effect, as well as a lacunar infarct in the left corona radiata. She was not a candidate for endovascular thrombectomy nor thrombolysis and medical management was pursued. The etiology of her stroke was initially unclear. Carotid CTA showed no significant stenosis. As per the assessment by neurology, her stroke was possibly explained by a hypercoagulable state in the setting of cancer and recent surgery versus possible cardioembolic cause, although she had been monitored with telemetry overnight and was noted to be in sinus rhythm. Subsequently, on POD 2, she developed documented atrial fibrillation with rapid ventricular rate as well as progressive mixed respiratory failure in the setting of volume overload and mucus plugging. With hindsight, her stroke was likely embolic, secondary to new onset atrial fibrillation in the postoperative period, and she was started on anticoagulation for secondary stroke prevention when it was safe to do so. In previous literature, atrial fibrillation has been a consistent risk factor for perioperative stroke, not only after thoracic surgery but also across a variety of surgical populations[6]. With regards to deficits at the time of discharge, she had ongoing right homonymous hemianopsia but no other deficits and she received ongoing follow-up as an outpatient with Ophthalmology and with the Stroke Prevention Clinic.

Discussion: There is emerging research demonstrating the potential role of covert perioperative stroke in postoperative delirium and cognitive function[5]. We present a case of perioperative stroke in which the initial presentation was confusion on POD1, which may have easily been mistaken for postoperative delirium. Despite limited options for treatment of her stroke because of the location of her stroke and timing relative to major surgery, we were able to implement stroke rehabilitation as well as appropriate follow-up with the Stroke Prevention Clinic. We hope that additional descriptions of perioperative stroke will continue to lead to increased awareness of this complication, early diagnosis, prompt treatment, and implementation of secondary prevention strategies that are essential in improving patient outcomes in the perioperative setting.

References:

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Feasibility trial of remotely delivered prehabilitation program in colorectal cancer patients.

Presenter: Derek Dionne
Research Supervisor: Jordan Leitch
Collaborators: Taryn Davidson, Selim Choi, Benjamin Larocque, Janet van Vlymen, Melanie Jaeger, Sunil Patel, Anil Farooq.

Abstract:
Colorectal cancer is one of the most prevalent malignancies worldwide with a substantial impact on patient morbidity and mortality. Patients often undergo surgical resection as part of their initial treatment, which is a major psychological and physiological stressor. Prehabilitation involves prescribed preoperative interventions like exercise, nutrition, and mindfulness. It has emerged as a strategy to improve surgical outcomes and postoperative recovery. This pilot study aims to determine the feasibility of a remotely monitored, trimodal prehabilitation program for colorectal cancer patients at KHSC. We used a web application, CloudDX, to monitor patient adherence to our pilot prehabilitation program. This study is a non-blinded parallel arm randomized control trial. We aim to enroll 25 participants undergoing colorectal surgery for malignancy; patients will be randomly assigned to one of two groups: 1) prehabilitation with phone call progress checks from one of the investigators and 2) prehabilitation without progress checks. All patients are given information on completing the trimodal program, which includes six times per week strength and aerobic exercise; a basic nutrition program to achieve 1.2grams of protein per 1.2kg body weight and twice daily breathing exercises. Requested activities were tracked daily via the online platform. We assessed feasibility outcomes including the weeks available for prehabilitation before surgery, patient satisfaction with program and adherence to program. Our preliminary findings include compliance of 62% with check- in vs 44% without check-in for completion of activity tracker, in percentage of days available prior to surgery, with no significant difference between groups. The range of available days from initiating program to surgical date was minimum 6 days up to 50 days, an average of 24 days for prehabilitation. Further data analysis upcoming. This investigation may provide clinically useful insights into the practical implementation and potential benefits of a prehabilitation program, shaping future research and clinical practice in perioperative care.

An epidemiological study of the circadian control of biopsychosocial outcomes in chronic pain

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Introduction: 20% of the Canadian population lives with chronic pain, which is the leading contributor to years lived with disability and disease burden worldwide[1]. Despite its ubiquity, current therapeutics for chronic pain are lacking. To develop more effective treatment strategies, it is crucial to know *when* and *why* someone has pain. Thus, pain fluctuations represent an interesting research target. Time-dependent fluctuations in acute thermal nociception have been found to be regulated by majority endogenous circadian rhythms and not sleep/wake cycles[2]. Thus, we hypothesize that circadian rhythms also play a role in mechanisms of chronic pain. Our study (CircaPain) explored how rhythmicity of pain intensity may be associated with well-being.

Methods: Canadian adults with chronic pain (≥3 months) were recruited for this cross-sectional study (n=897). Following an initial questionnaire, participants completed electronic symptom-tracking diaries (ecological momentary assessments; EMA), in which they rated their pain intensity, affect, and fatigue on a 0-10 scale at 3 timepoints (08:00, 14:00, 20:00) daily for 1 week. EMA pain intensity data were used to identify phenotypic patterns of pain rhythmicity. Differential clustering was investigated via latent class mixed effect modelling[3] and functional data analysis[4].

Results: Five key phenotypes of pain rhythmicity were identified using mean pain scores and 30% daily change as distinguishing features: constant low (23.0% of total), constant high (27.0%), rhythmic↑ (16.0%) or rhythmic↓ (4.1%), and mixed (arrhythmic; 29.9%). Despite rhythmic↑ participants reporting similar pain intensities in the evening to constant high participants, they reported improved measures associated with well-being. Notably, the rhythmic↑ group (n=102) reported significantly less pain interference in daily activities ($p=0.0066$), fatigue ($p=0.0225$), and depressive symptoms ($p<0.0001$) than the constant high group (n=172).

Discussion: The associations between diverse pain phenotypes and well-being measures observed in our sample present a tool to characterise and potentially help manage chronic pain. Our epidemiological project will be complemented by a follow-up study encompassing the collection of blood from participants at multiple times of day to explore potential biomarkers of pain rhythmicity. (This work is supported by CIHR and the CIHR-SPOR Chronic Pain Network.)

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What complications relevant to emergent airway management have been reported in patients with achalasia in the literature?

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Background

Achalasia is an uncommon primary esophageal motor disorder, with an incidence estimated at 1.63/100,000 and prevalence of 10.82/100,000 in Canada[1]. Given the treatment of this disorder often involves surgical and/or endoscopic myotomy or dilatations[2], these patients are likely to be encountered by the anesthesiologist. It understood that achalasia is associated with respiratory symptoms such as cough, dyspnea, and puts patients at risk of pulmonary aspiration of esophageal contents. Many case studies exist describing respiratory distress due to a megaesophagus phenomenon in achalasia[4-8]. However, to our knowledge, there has only been one summary of these case reports in the literature[9], focusing on plausible mechanistic explanations of the phenomenon, and not considerations pertinent to the anesthesiologist, such as hemodynamic changes from thoracic inlet obstruction[8] and potential for compression associated reccurent laryngeal nerve palsy[7].

Study design and Update:

This narrative review summarizes available reports of tracheal distortion with achalasia. After consultation with a librarian, a literature search utilizing the OVID interface to access the Medline and Embase databases was performed, with 603 articles resulting after duplicates were removed. Title and abstract screening of the articles for relevancy, with a resulting 73 being included for full-text screening. Additionally, the citation list of these 73 articles were screened for potentially relevant articles not captured in our database search, resulting in an additional 54 articles included for full-text screening. After full-text screening for relevancy (emergency airway management in megaesophagus cases), 68 of 127 articles undergoing full text screening were included for data extraction. Early data analysis shows a trend of patients with megaesophagus associated tracheal compression being older (mean age 69.2 years, IQR 56-82), female (85.3%), and in obvious respiratory distress (94.1%).

Next steps:

Data extraction remains ongoing, nearing its completion. Data analysis, knowledge synthesis, and knowledge dissemination constitute next steps.

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Endotracheal tube anatomy and endobronchial intubation - are Parker Flex-Tip ETTs less prone to right mainstem endobronchial intubation than standard tip ETTs?

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Lung isolation and one-lung ventilation is often required in thoracic surgery, and is occasionally needed in emergencies, such as massive pulmonary hemorrhage. In elective thoracic surgery, when time is permits, a double-lumen endotracheal/endobronchial tube (DLT) is often used, with placement aided by fiberoptic bronchoscopy (1). However, in an emergency situation, rapid fiberoptic bronchoscopic intubation with a DLT may be difficult to perform safely and effectively, requiring alternative techniques for lung isolation and one-lung ventilation (1). In these situations, the use of a single-lumen endotracheal tube (SLT), with or without a bronchial blocker, can be used to facilitate lung isolation and one-lung ventilation.
In the instance of intubation with an SLT *without* use of a bronchial blocker, in order to effectively isolate the lungs for one-lung ventilation the SLT must be advanced into a mainstem bronchus, resulting in endobronchial intubation. Furthermore, to effectively isolate the lungs, and provide ventilation to the non-soiled lung, the SLT must be inserted into the desired (correct) mainstem bronchus (typically, the mainstem bronchus of the non-soiled lung).

Due to the anatomic structure of the tracheobronchial tree, left endobronchial intubation is not easily performed in isolation, using an SLT, without fiberoptic bronchoscopic confirmation (1). A variety of techniques have been developed (1-3) in order to attempt to improve first-pass intubation success in difficult situations, or to effectively intubate the left mainstem bronchus. Similarly, a variety of endotracheal tubes have been developed (4) for managing a variety of challenging airway situations.

One of the more recent endotracheal tube varieties is the Parker Flex-Tip endotracheal tube (PFT) (4). It has been developed with a smoother, and more curved tip, with the idea being that it may facilitate passage into the airway with a lower chance of becoming caught on various anatomical structures. Several studies have attempted to determine whether the PFT does, in fact, confer benefit in a variety of airway management situations. Specifically, Yamauchi & colleagues (6) found that it facilitated intubation via fiberoptic bronchoscopy in pulmonologists with limited experience. Several studies (6,7) found the PFT improved speed and/or first-pass success on intubation, while another study (8) found that in direct-laryngoscopy nasal intubations, PFTs had a lower incidence of impingement on airway structures compared to standard ETTs. However, similar studies have found no benefit conferred by the PFT in nasal intubations (9), fiberoptic orotracheal intubation in obese patients (10), or in simulated front of neck percutaneous emergency airway management (11).

The techniques that have been developed to selectively intubate the left mainstem bronchus using an SLT depend, at least in part, on the use and manipulation of the bevel of the ETT, with respect to the main carina. Given the altered, curved tip design of the PFT, it may not perform in a similar manner to standard-bevel ETTs for intentional left mainstem endobronchial intubation.

The goal of this study is to examine how the PFT performs for selective left mainstem endobronchial intubation under similar techniques that have been previously described (1-3).

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Genicular **E**mbolization vs. **N**eurolysis **I**ntervention for knee osteoarthritis: protocol for the GENI Knee OA study

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Funding: This work is supported by the SEAMO Innovation Fund, the SEAMO CTAQ Research Endowment Fund, and the Queen's Department of Diagnostic Radiology. KN is supported by the Vandewater Studentship.

Knee osteoarthritis (OA) is a common and debilitating disease affecting 22.9% of adults aged 40 and over worldwide.[1] Currently, the best way to treat advanced disease that is resistant or refractory to non-surgical options is with total knee arthroplasty (TKA). Instances when surgical options are not readily available represents a specific management challenge. Genicular artery embolization (GAE) and phenol genicular nerve ablation (PNA) have emerged as potentially successful treatments to reduce knee OA symptoms.[2-3] However, to our knowledge, no randomized controlled trials directly comparing the two procedures have been completed to date.

This three-arm prospective randomized controlled trial will compare clinical outcomes of GAE with genicular nerve PNA in patients with knee OA awaiting TKA at KHSC. Specifically, the study questions are: (1) How does GAE compare to genicular nerve PNA with regard to OA symptom reduction, and how do these procedures compare to sham procedure? (2) Are there any changes to imaging and biochemical in response to GAE or genicular nerve PNA? (3) Are there any side effects or changes in: knee-specific analgesia use, willingness to undergo TKA, and activity level following GAE or genicular nerve PNA?

Over approximately 24 months, 150 patients will be recruited from orthopedic surgery clinics at KHSC. Those who satisfy the eligibility criteria will be enrolled and randomized to receive either GAE, genicular nerve PNA, or sham procedure. This study involves three in-person appointments within the span of 3-4 months; a baseline assessment, procedure appointment, and follow-up assessment. Participants will then be contacted for follow-up every 6 months for the next 2 years or until they undergo TKA, whichever comes first.

Knee 3T MRI with gadolinium and 0.5-5cc synovial fluid aspiration will be completed at baseline and 3 months to compare imaging and biochemical markers pre- and post-procedure. Monitoring of pain, stiffness, and function will occur using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and numerological rating scale (NRS) scores at baseline, 3 months, 6 months, and every 6 months thereafter for two years or until TKA surgery. Procedure side effects, knee-specific analgesia use, willingness to undergo TKA, and activity level will also be collected at each time point. Findings from this work are anticipated to inform best practices in the management of advanced knee OA in patients who qualify for TKA at KHSC.

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Cardiac Changes after Low Dose Carbetocin for Elective Caesarian Section

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Background

Carbetocin is commonly used for the prevention of post-partum hemorrhage (PPH), and is recommended as a first line agent by the Society of Obstetrics and Gynecology of Canada for PPH prophylaxis in Caesarian section (CS). Currently dose recommendations are 100mcg of carbetocin for all patients undergoing elective CS[1]. However, recently evidence found the ED90 of carbetocin for the prevention of PPH in non-labouring, non-obese patients to be only 14.9mcg[2]. Despite its widespread use carbetocin is not without its side effects and disadvantages[3]. Previously recommended doses of the shorter acting oxytocin have been shown to cause coronary vasospasm, resulting in chest pain EKG changes and increased troponins. Similarly, chest pain is a reported side effect of the administration of the longer acting carbetocin, current studies found rates to be 2/52 after administration of 100mcg during elective CS[4]. Beyond subjective symptoms, carbetocin has been found to cause hemodynamic and ECG changes. Carbetocin has been associated with increases in heart rate, decreases in blood pressure and increases in the QTc interval when given at a dose of 100mcg[4,5].

Rationale

Research into the subjective and objective cardiac changes after carbetocin administration is relatively sparse and mostly limited to doses of 100mcg. Given emerging evidence supporting lower doses of carbetocin for effective PPH prophylaxis, more data is required regarding the efficacy of low-dose carbetocin, patient reported side effects and objective markers of cardiac changes. In this study we will examine the rates of patient reported cardiac symptoms, ECG changes and troponin increases after administration of low dose carbetocin (50mcg) compared to standard dose carbetocin (100mcg). Further, we will examine the relationship between patient-reported symptoms and objective markers of cardiac changes (ECG changes and troponin increase). We believe that significant findings in this study may necessitate updating of the current recommend dosing of carbetocin. Finally, biochemical or ECG findings suggestive of cardiac changes after carbetocin administration would necessitate further study, as this may confer an increased risk of perioperative morbidity and mortality akin to that of myocardial injury after non-cardiac surgery (MINS), a known risk for vascular morbidity and death in the non-obstetric population[6].

Study Design

This is a pilot, single-center double-blind randomized control trial that will determine rates of subjective cardiac symptoms, troponin increases and ECG changes between participants receiving 50mcg or 100mcg of carbetocin for PPH prophylaxis during elective CS. We will be including participants who are undergoing elective CS under neuraxial anesthesia and excluding those with an elevated BMI and those with pre-existing cardiac conditions. Participants will be randomized into two groups and will be given either 50mcg or 100mcg of carbetocin for PPH prophylaxis at the time of umbilical cord clamping during their CS. Data surrounding patient reported symptoms, ECG changes and markers of PPH will be collected during the CS. Immediately after and six hours after the CS, a troponin will be drawn. Finally, a chart review will be conducted for relevant medical and obstetrical history including estimated blood loss and change in postoperative Hemoglobin as a safety end point.

Current Progress

This project is currently in the project proposal stage. Ethics and funding submissions are underway and expected to be submitted within the month.

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Microglial activation is regulated by circadian rhythms in chronic neuropathic pain

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Background:

Microglia have been shown to be drivers of pain hypersensitivity in the spared nerve injury model of neuropathic pain in mice[1]. Following SNI, microglia in the dorsal horn of the spinal cord proliferate and transition from a homeostatic phenotype to a pro-inflammatory phenotype, potentially in a sex-dependent manner. These microglia have been shown to retain their morphology and pro-inflammatory phenotype from acute to chronic timepoints (>3 months)[2]. Cellular changes in microglia are accompanied by behavioural changes as mice develop mechanical and thermal (cold) allodynia, which they retain into the chronic phase. Research has now shown that microglial gene expression patterns, activation states, and physiological function are governed by circadian (24-hour) rhythms, with diverse regional heterogeneity[3]. Clinical studies have also shown that pain can be rhythmic in various chronic pain states[4]. However, it remains unknown whether microglia exhibit circadian rhythmicity in chronic pain.

Methods:

To investigate this gap in knowledge, male and female C57BL/6J mice received a spared nerve injury, with tissues collected at 3, 7, 10, 14, 28, and 84 days following injury. Animals were sacrificed at ZT2 (rest phase) and ZT14 (active phase), corresponding to 2 hours after start of the light and dark period on each collection day. Cryostat sections of the spinal cord were immunostained for markers of homeostatic and pro-inflammatory microglia, as well as transcriptional regulators known to be under circadian control. Confocal z-stacks were taken to create 3D surface renderings of cells, with surface renderings analyzed to characterize microglial morphology and activation state. Data collected include changes in cell volume, lysosomal volume, and process length and ramification, which are characteristic changes in microglial response to injury and pain. The experiments were repeated using *Cx3cr1*^{CreER}; *Bmal1* $^{flox/flox}$ mice, in which clock gene *Bmal1* is specifically ablated in microglia.

Results:

We found rhythmic changes in both microglial morphology and activation state in both the naïve and injured state. In the naïve state, microglia exhibited more ramified, extended processes indicative of a homeostatic surveillance phenotype during the dark (active) phase. Meanwhile, microglia had shorter, less ramified processes and morphology indicative of a pro-inflammatory phenotype in the light (rest) phase. During peak periods of microglial activation following SNI, which occur between 7- and 14-days following injury, microglia in the dorsal horn took on an extremely pro-inflammatory phenotype during the light phase but retained a more homeostatic phenotype during the dark phase relative to the light-phase in injured animals. In mice with *Bmal1* conditionally knocked out in microglia, the morphological changes between time points were less distinct.

Conclusions:

Our work indicates that in both the naïve and post-SNI spinal cord, microglia undergo changes in their gene expression, morphology, and function over a 24-hour cycle, and that disruption of circadian gene expression machinery affects microglial activation patterns. As microglia have been shown to the development of chronic pain, understanding microglial activation states across male and female mice, and during the circadian cycle, may provide new insight into mechanisms regulating their activity and function in the pathophysiology of chronic neuropathic pain.

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Real-Time Remote Supervision and Teaching for Regional Anesthesia (Update)

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Regional anesthesia, a major advancement in anesthesia, has led to significant improvements in multiple facets of perioperative care including reduced perioperative opioid consumption, reduced hospital length of stay, reduced healthcare costs, and improved patient satisfaction. With the increasing availability of ultrasound, the use of regional anesthesia has greatly increased, however, is not yet ubiquitous among surgical centres. Uptake of regional techniques outside of academic centres is limited by the availability of experts to provide one-on-one training opportunities. With the adoption of virtual teaching in many other aspects of medical education, there-in-lies an opportunity to implement real-time remote regional anesthesia training, allowing for improved dissemination of expert guidance and training.

Our study aims to develop, implement, and evaluate the use of a real-time remote teaching and learning method for training in regional anesthesia. Using wireless ultrasound technology we will evaluate the ability of trainee physicians to perform standard-of-care regional techniques while supervised remotely by export mentors. Specifically, our study will utilize trainees in regional nerve blocks (senior anesthesiology/emergency medicine residents or emergency medicine staff physicians), supervised by experts in regional techniques (anesthesiology staff). Nerve blocks will be performed on patients scheduled for elective surgery at Kingston General Hospital or Hotel Dieu Hospital, or those presenting to the KGH emergency department, who would benefit from a regional nerve block in their management course. Using wireless linear ultrasounds (Clarius) that connect to iPads and iPhones, we will create an environment in which mentors can safety supervise and mentor trainees from a distance as they perform their blocks.

Qualitative data collection will be performed after completion of each block; trainees and mentors will be asked to rate their experience with remove supervision/teaching through a questionnaire. Additionally, we will complete voluntary focus group sessions regarding their experiences and potential for implementation into clinical practice. Statistical analysis will be performed using appropriate techniques for qualitative data collected from each questionnaire and thematic analyses from each focus group. We hope this study can help in developing a safe and practical method to expand regional training beyond the borders of high-resource settings.

IV Dexmedetomidine in Cesarean Section: A Systematic Review

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Background: Dexmedetomidine has been gaining prominence as an adjunctive medication in obstetrical anesthesiology for many indications including anxiolysis, analgesia, anti-shivering and sedation. Both intravenous and neuraxial uses have been described in the literature, however, to date, no scoping or systematic review has been published on the topic, potentially limiting knowledge translation.
Knowledge Gap: No scoping or systematic literature review has been published on IV dexmedetomidine describing its safety, efficacy and indications in the obstetrical population.
Study Objective: To complete a systematic review of the use of IV dexmedetomidine in parturients undergoing cesarean section with neuraxial anesthetic.
Methods: The protocol for this systematic review was developed following the PRISMA-P guidelines will be registered with PROSPERO database. Eligible studies include parturients undergoing cesarean section under neuraxial anesthetic, in which at least one arm receives intravenous dexmedetomidine. All quantitative, qualitative and mixed methods studies will be eligible. Publication types including peer-reviewed articles, conference papers and abstracts, pre-print articles, and unpublished trial data will be eligible. No date restrictions will be applied, and publications in all languages will be eligible. The search strategy was developed in consultation with Queen's Librarians Sandra McKeown and Angelique Roy. A complete list of search terms and subject headings will be made available. Data will be managed in an Excel spreadsheet throughout the review. Embase, MEDLINE (Ovid), Cochrane Library and Web of Science will be searched. All eligible studies will be screened with Covidence to eliminate duplicates. Eligible studies will be screened by two independent reviewers for inclusion. Included studies will be assessed by two independent reviewers with the 2019 Cochrane Revised Risk of Bias tool (RoB2). The studies will have a qualitative narrative synthesis performed according to the Synthesis Without Meta-analysis (SWiM) reporting guideline. Finally, an overall quality of evidence will be assigned using the GRADE framework.
Next Steps: This study's results could be used to perform a meta-analysis on the topic. Furthermore, it could inform future studies on neonatal outcomes, effects of dexmedetomidine on uterine tone, intraoperative bleeding and to inform future qualitative studies on patient experience during cesarean section.

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Transcriptomics implicate neutrophil activity in the rhythmicity and chronicity of low back pain

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Background and Aims: Chronic low back pain (CLBP) is highly prevalent (~8% globally) and is the leading cause of years lived with disability worldwide. Previous work shows that peripheral immune cells, such as neutrophils, monocytes, and T cells, have a role in the chronicity of pain. Indeed, neutrophils have been suggested to relieve pain by secreting opioid peptides at the site of inflammation and inhibiting T-cell responses. Neutrophils have also been shown to have circadian rhythms in their gene expression and trafficking in the naïve and injured states. Likewise, CLBP has been shown to vary in intensity throughout the day; however, the mechanisms underlying this variability remain unclear at the molecular and cellular levels. This study aims to investigate how CLBP pain rhythmicity affects immune cells and the transcriptomic changes underlying their responses.

Methods: Pain rhythmicity phenotypes (constant-low, constant-high, rhythmic↑ and mixed) were characterized in 74 participants with CLBP. Peripheral blood samples (n=116) were collected at 8:00 and 20:00 for bulk RNA-sequencing. Reads were processed using *FastQC*/*MultiQC*, *Hisat2*, and *StringTie*. Normalization and outlier detection applied *edgeR* and *arrayQualityMetrics*. Transcripts with median absolute deviations ≥ the 70th quantile (n=101,0350) were kept for analysis. We identified differentially expressed transcripts (DETs) between the rhythmic↑ and other phenotypes using *edgeR*. Unsupervised network analysis identified transcript clusters associated with pain rhythmicity↑. G*profiler2* ran pathway analysis on significant transcripts. Using the PainOMICs LBP cohort to replicate results, *DESeq2* assessed whether a gene's trajectory between two visits differs between opioid users vs non-users. Enrichment analysis (*fgsea*) focused on Gene Ontology's biological processes (GO:BP) about cell activation.

Results: We identified 40 to 170 significant DETs between the rhythmic↑ and other pain phenotypes. Pathway analyses determined significant enrichment of immune cell signaling and neutrophil degranulation pathways. Network analysis clustered transcripts into 82 and 77 clusters of co-expressed transcripts in the day and night networks, respectively. The rhythmic↑ phenotype was associated with 3 "day" clusters and 5 "night" clusters. Further, the neutrophil degranulation pathway was enriched in a night cluster negatively associated with rhythmicity↑ ($P_{adj.}$<10e-57). Moreover, among all cell types of hematopoietic origin whose activation pathway were documented in GO:BP, only neutrophils showed significant activation. Finally, the neutrophil degranulation pathway's genes were over-expressed over time in opioid users versus non-users (enrichment score +0.31, P=2e-6).

Conclusions: Our results suggest that neutrophil activation may differentiate the rhythmic↑ pain phenotype, and potentially non-opioid users, from other pain phenotypes. Specifically, there is less neutrophil degranulation amongst patients with a rhythm of CLBP intensity and amongst those who do not consume opioids. These findings support previous evidence that neutrophils play a role in chronic pain and are under circadian control. However, the role of neutrophil activation in the rhythmicity of pain intensity has not previously been described. Hence, circadian rhythms of pain and neutrophil activation may guide novel interventions for individuals with chronic low back pain.

Funding: CIHR-SPOR Chronic Pain Network, CIHR

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